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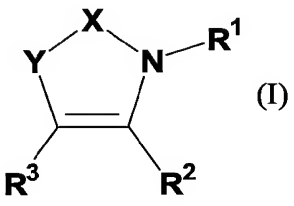
(54) Title: NOVEL PYRIDINONE DERIVATIVES AND THEIR USE AS POSITIVE ALLOSTERIC MODULATORS OF MGLUR2-RECEPTORS



(I)

(57) Abstract: The present invention relates to novel compounds, in particular novel pyridinone derivat ives according to Formula (I) X R1 N Y (I) R2 R3 wherein all radicals are defined in the application. The compounds according to the invention are positive allosteric modulators of metabotropic receptors - subt ype 2 ("mGluR2") which are useful for the treatment or prevention of neurological and psychiatric disorders associated with glutamate dysfunction and diseases in which the mGluR2 subtype of metabotropic receptors is involved. In particular, such diseases are central nervous system disorders selected from the group of anxiety, schizophrenia, migraine, depression, and epilepsy. The invention is also directed to pharmaceutical compositions and processes to prepare such compounds and compositions, as well as to the use of such compounds for the prevention and treatment of such diseases in which mGluR2 is involved.

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NOVEL PYRIDINONE DERIVATIVES AND THEIR USE AS POSITIVE ALLOSTERIC MODULATORS OF MGLUR2-RECEPTORS

SUMMARY OF THE INVENTION

The present invention relates to novel compounds, in particular novel pyridinone-derivatives that are positive allosteric modulators of metabotropic receptors – subtype 2 ("mGluR2") which are useful for the treatment or prevention of neurological and psychiatric disorders associated with glutamate dysfunction and diseases in which the mGluR2 subtype of metabotropic receptors is involved. The invention is also directed to the pharmaceutical compositions, the processes to prepare such compounds and compositions and the use of such compounds for the prevention and treatment of such diseases in which mGluR2 is involved.

BACKGROUND OF THE INVENTION

Glutamate is the major amino-acid transmitter in the mammalian central nervous system (CNS). Glutamate plays a major role in numerous physiological functions, such as learning and memory but also sensory perception, development of synaptic plasticity, motor control, respiration, and regulation of cardiovascular function. Furthermore, glutamate is at the centre of several different neurological and psychiatric diseases, where there is an imbalance in glutamatergic neurotransmission.

Glutamate mediates synaptic neurotransmission through the activation of ionotropic glutamate receptors channels (iGluRs), the NMDA, AMPA and kainate receptors which are responsible for fast excitatory transmission (Nakanishi et al., (1998) Brain Res Brain Res Rev., 26:230-235).

In addition, glutamate activates metabotropic glutamate receptors (mGluRs) which have a more modulatory role that contributes to the fine-tuning of synaptic efficacy.

The mGluRs are seven-transmembrane G protein-coupled receptors (GPCRs) belonging to family 3 of GPCRs along with the calcium-sensing, GABAb, and pheromone receptors.

Glutamate activates the mGluRs through binding to the large extracellular amino-terminal domain of the receptor, herein called the orthosteric binding site. This binding induces a conformational change in the receptor which results in the activation of the G-protein and intracellular signalling pathways.

The mGluR family is composed of eight members. They are classified into three groups (group I comprising mGluR1 and mGluR5; group II comprising mGluR2 and mGluR3; group III comprising mGluR4, mGluR6, mGluR7, and mGluR8) according to sequence homology, pharmacological profile, and nature of intracellular signalling cascades activated (Schoepp et al. (1999) Neuropharmacology, 38:1431-76).

Among mGluR members, the mGluR2 subtype is negatively coupled to adenylate cyclase via activation of Gαi-protein, and its activation leads to inhibition of glutamate release in the synapse (Cartmell & Schoepp (2000) J Neurochem 75:889-907). In the CNS, mGluR2 receptors are abundant mainly throughout cortex, thalamic regions, accessory olfactory bulb, hippocampus, amygdala, caudate-putamen and nucleus accumbens (Ohishi et al. (1998) Neurosci Res 30:65-82).

Activating mGluR2 was shown in clinical trials to be efficacious to treat anxiety disorders (Levine et al. (2002) Neuropharmacology 43: 294 ; Holden (2003) Science 300:1866-68; Grillon et al. (2003) Psychopharmacology 168:446–54 ; Kellner et al. (2005) Psychopharmacology 179: 310–15). In addition, activating mGluR2 in various animal models was shown to be efficacious, thus representing a potential novel therapeutic approach for the treatment of schizophrenia (reviewed in Schoepp & Marek (2002) Curr Drug Targets. 1:215-25), epilepsy (reviewed in Moldrich et al. (2003) Eur J Pharmacol. 476:3– 16), migraine (Johnson et al. (2002) Neuropharmacology 43:291), addiction/drug dependence (Helton et al. (1997) J Pharmacol Exp Ther 284: 651-660), Parkinson's disease (Bradley et al (2000) J Neurosci. 20(9):3085-94), pain (Simmons et al. (2002) Pharmacol Biochem Behav 73:419–27), sleep disorders (Feinberg et al. (2002) Pharmacol Biochem Behav 73:467–74) and Huntington's disease (Schiefer et al. (2004) Brain Res 1019:246-54).

To date, most of the available pharmacological tools targeting mGluRs are orthosteric ligands which activate several members of the family as they are structural analogs of glutamate (Schoepp et al. (1999) Neuropharmacology, 38:1431-76).

A new avenue for developing selective compounds acting at mGluRs is to identify molecules that act through allosteric mechanisms, modulating the receptor by binding to a site different from the highly conserved orthosteric binding site.

Positive allosteric modulators of mGluRs have emerged recently as novel pharmacological entities offering this attractive alternative. This type of molecule has been discovered for several mGluRs (reviewed in Mutel (2002) Expert Opin. Ther. Patents 12:1-8). In particular molecules have been described as mGluR2 positive allosteric modulators (Johnson MP et al. (2003) J Med Chem. 46:3189-92; Pinkerton et al. (2004) J Med Chem. 47:4595-9).

WO2004092135 (NPS & Astra Zeneca), WO04018386 (Merck) and WO0156990 (Eli Lilly) describe respectively phenyl sulfonamid, acetophenone and pyridylmethyl sulfonamide derivatives as mGluR2 positive allosteric modulators. However, none of the specifically disclosed compounds are structurally related to the compounds of the invention.

It was demonstrated that such molecules do not activate the receptor by themselves (Johnson MP et al. (2003) J Med Chem. 46:3189-92; Schaffhauser et al. (2003) Mol Pharmacol. 64:798-810). Rather, they enable the receptor to produce a maximal response to a concentration of glutamate which by itself induces a minimal response. Mutational analysis have demonstrated unequivocally that the binding of mGluR2 positive allosteric modulators does not occur at the orthosteric site, but instead at an allosteric site situated within the seven transmembrane region of the receptor (Schaffhauser et al. (2003) Mol Pharmacol. 64:798-810).

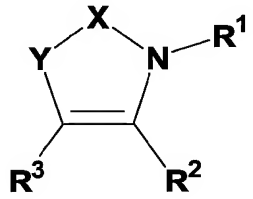
Animal data are suggesting that positive allosteric modulators of mGluR2 have the same effects in anxiety and psychosis models as those obtained with orthosteric agonists. Allosteric modulators of mGluR2 were shown to be active in fear-potentiated startle (Johnson et al. (2003) J Med Chem. 46:3189-92; Johnson et al. (2005) Psychopharmacology 179:271-83), and in stress-induced hyperthermia (Johnson et al. (2005) Psychopharmacology 179:271-83) models of anxiety. Furthermore, such compounds were shown to be active in reversal of ketamine- (Govek et al. (2005) Bioorg Med Chem Lett 15(18):4068-72) or amphetamine- (Galici et al. (2005) J Pharm Exp Ther Fast Forward, 2005 Aug 25, Epub ahead of print) induced hyperlocomotion,

and in reversal of amphetamine-induced disruption of prepulse inhibition of the acoustic startle effect (Galici et al. J Pharm Exp Ther Fast Forward, 2005 Aug 25, Epub ahead of print) models of schizophrenia.

Positive allosteric modulators enable potentiation of the glutamate response, but they have also been shown to potentiate the response to orthosteric mGluR2 agonists such as LY379268 (Johnson et al. (2004) Biochem Soc Trans 32:881-87) or DCG-IV (Poisik et al. (2005) Neuropharmacology 49:57-69). These data provide evidence for yet another novel therapeutic approach to treat above mentioned neurological diseases involving mGluR2, which would use a combination of a positive allosteric modulator of mGluR2 together with an orthosteric agonist of mGluR2.

DETAILED DESCRIPTION OF THE INVENTION

The invention relates to compounds having metabotropic glutamate receptor 2 modulator activity. In its most general compound aspect, the present invention provides a compound according to Formula (I),



(I)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

X is selected from C(=O), S(O), $S(O)_2$, $C(=NR^6)$ and C(=S);

Y is selected from S, $-C(R^4)=C(R^5)-$, $-C(R^5)=N-$, $-N=C(R^5)-$ and $-N(R^5)-$;

R^1 is not hydrogen and is an optionally substituted radical selected from the group of -$(C_1$-$C_6)$alkyl, -$(C_2$-$C_6)$alkynyl, -$(C_2$-$C_6)$alkenyl, -$(C_3$-$C_7)$cycloalkyl, -$(C_3$-$C_8)$cyclo-alkenyl, -$(C_1$-$C_6)$alkylhalo, -$(C_1$-$C_6)$alkylcyano and a radical $-V_1$-T_1-M_1;

T_1, V_1 are each independently a covalent bond or an optionally substituted radical selected from the group of -$(C_1$-$C_6)$alkyl-, -$(C_2$-$C_6)$alkynyl-, -$(C_2$-$C_6)$alkenyl-, -$(C_3$-$C_7)$-cycloalkyl-, -$(C_4$-$C_{10})$alkylcycloalkyl-, -$(C_3$-$C_8)$cycloalkenyl-, -$(C_1$-$C_6)$alkylhalo-, -$(C_1$-

C_6)alkylcyano-, -(C_1-C_6)alkyl-C(=O)-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-C(=O)-(C_2-C_6)-alkynyl-, -(C_1-C_6)alkyl-C(=O)-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-C(=O)-(C_3-C_7)-cycloalkyl-, -(C_1-C_6)alkyl-C(=O)-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-C(=O)O-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-C(=O)O-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-C(=O)O-(C_2-C_6)-alkenyl-, -(C_1-C_6)alkyl-C(=O)O-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-C(=O)O-(C_4-C_{10})-alkylcycloalkyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-O-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-O-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-O-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-O-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-O-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)-alkyl-S-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-S-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-S-(C_2-C_6)-alkenyl-, -(C_1-C_6)alkyl-S-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-S-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-S(O)-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-S(O)-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-S(O)-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-S(O)-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-S(O)-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-$S(O)_2$-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-$S(O)_2$-(C_2-C_6)-alkynyl-, -(C_1-C_6)alkyl-$S(O)_2$-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-$S(O)_2$-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-$S(O)_2$-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-$S(O)_2NR^7$-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-$S(O)_2NR^7$-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-$S(O)_2NR^7$-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-$S(O)_2NR^7$-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-$S(O)_2NR^7$-(C_4-C_{10})alkyl-cycloalkyl-, -(C_1-C_6)alkyl-NR^7-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-NR^7-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-NR^7-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-NR^7-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=O)-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7C(=O)-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-NR^7C(=O)-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-NR^7C(=O)-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=O)-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=O)NR^8-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7C(=O)NR^8-(C_2-C_6)-alkynyl-, -(C_1-C_6)alkyl-NR^7C(=O)NR^8-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-NR^7C(=O)NR^8-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=O)NR^8-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)-alkyl-$NR^7S(O)_2$-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-$NR^7S(O)_2$-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-$NR^7S(O)_2$-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-$NR^7S(O)_2$-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-$NR^7S(O)_2$-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=S)NR^8-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7C(=S)NR^8-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-NR^7C(=S)NR^8-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-NR^7C(=S)NR^8-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=S)NR^8-(C_4-

C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-OC(=O)-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-OC(=O)-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-OC(=O)-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-OC(=O)-(C_3-C_7)-cycloalkyl-, -(C_1-C_6)alkyl-OC(=O)-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-OC(=O)NR^7-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-OC(=O)NR^7-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-OC(=O)NR^7-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-OC(=O)NR^7-(C_3-C_7)cycloalkyl-, -(C_1-C_6)-alkyl-OC(=O)NR^7-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=O)O-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7C(=O)O-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-NR^7C(=O)O-(C_2-C_6)-alkenyl-, -(C_1-C_6)alkyl-NR^7C(=O)O-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=O)O-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=NR^8)NR^9-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7C(=NR^8)NR^9-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-NR^7C(=NR^8)NR^9-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-NR^7C(=NR^8)NR^9-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=NR^8)NR^9-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=NR^8)-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7C(=NR^8)-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-NR^7C(=NR^8)-(C_2-C_6)alkenyl-, -(C_1-C_6)-alkyl-NR^7C(=NR^8)-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=NR^8)-(C_4-C_{10})-alkylcycloalkyl-, -(C_1-C_6)alkyl-C(=NR^7)NR^8-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-C(=NR^7)NR^8-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-C(=NR^7)NR^8-(C_2-C_6)alkenyl-, -(C_1-C_6)-alkyl-C(=NR^7)NR^8-(C_3-C_7)cycloalkyl- and -(C_1-C_6)alkyl-C(=NR^7)NR^8-(C_4-C_{10})-alkylcycloalkyl-;

R^2, R^3, R^4, R^5 and R^6 are each independently selected from the group of hydrogen, halogen, -CN, -OH, -NO_2, -CF_3, -NH_2, -SH, -C(=NR^{10})$NR^{11}R^{12}$, -C(=O)R^{10}, -C(=NR^{10})R^{11}, -C(=O)OR^{10}, -C(=O)$NR^{10}R^{11}$, -SR^{10}, -S(O)R^{10}, -$S(O)_2R^{10}$, -$NR^{10}R^{11}$, -NR^{10}C(=O)R^{11}, -NR^{10}C(=NR^{11})R^{12}, -NR^{10}C(=NR^{11})$NR^{12}R^{13}$, -NR^{10}C(=O)OR^{11}, -NR^{10}C(=O)$NR^{11}R^{12}$, -$NR^{10}S(O)_2R^{11}$, -$S(O)_2NR^{10}R^{11}$, -C(=S)$NR^{10}R^{11}$, -OC(=O)R^{10}, -OC(=O)$NR^{10}R^{11}$, -OR^{10}, and an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_1-C_6)alkylhalo, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)-cycloalkyl, -(C_3-C_8)cycloalkenyl, -(C_1-C_6)alkylcyano, -(C_1-C_6)alkylaryl, -(C_1-C_6)-alkylheteroaryl, aryl, heteroaryl and a radical -V_2-T_2-M_2;

T_2, V_2 are each independently a covalent bond or a radical selected from the group of -O-, -C(=O)-, -C(=O)O-, -C(=O)NR^{10}-, -S-, -S(O)-, -$S(O)_2$-, -$S(O)_2NR^{10}$-, -NR^{10}-, -NR^{10}C(=O)-, -NR^{10}C(=O)NR^{11}-, -$NR^{10}S(O)_2$-, -NR^{10}C(=S)NR^{11}-, -OC(=O)-, -OC(=O)NR^{10}, -NR^{10}C(=O)O-, and an optionally substituted radical selected from the group of -(C_1-C_6)alkyl-, -(C_2-C_6)alkynyl-, -(C_2-C_6)alkenyl-, -(C_3-C_7)cycloalkyl-, -(C_3-

C_8)cycloalkenyl-, -(C_1-C_6)alkylhalo-, -(C_1-C_6)alkylcyano-, -(C_0-C_6)alkyl-O-(C_1-C_6)-alkyl-, -(C_0-C_6)alkyl-O-(C_2-C_6)alkynyl-, -(C_0-C_6)alkyl-O-(C_2-C_6)alkenyl-, -(C_0-C_6)-alkyl-O-(C_3-C_7)cycloalkyl-, -(C_0-C_6)alkyl-O-(C_4-C_{10})alkylcycloalkyl-, -(C_0-C_6)alkyl-C(=O)-(C_1-C_6)alkyl-, -(C_0-C_6)alkyl-C(=O)-(C_2-C_6)alkynyl-, -(C_0-C_6)alkyl-C(=O)-(C_2-C_6)alkenyl-, -(C_0-C_6)alkyl-C(=O)-(C_3-C_7)alkylcycloalkyl-, -(C_0-C_6)alkyl-C(=O)-(C_4-C_{10})cycloalkyl-, -(C_0-C_6)alkyl-C(=O)O-(C_1-C_6)alkyl-, -(C_0-C_6)alkyl-C(=O)O-(C_2-C_6)-alkynyl-, -(C_0-C_6)alkyl-C(=O)O-(C_2-C_6)alkenyl-, -(C_0-C_6)alkyl-C(=O)O-(C_3-C_7)-cycloalkyl-, -(C_0-C_6)alkyl-C(=O)O-(C_4-C_{10})alkylcycloalkyl-, -(C_0-C_6)alkyl-C(=O)NR^{10}-(C_1-C_6)alkyl-, -(C_0-C_6)alkyl-C(=O)NR^{10}-(C_2-C_6)alkynyl-, -(C_0-C_6)alkyl-C(=O)NR^{10}-(C_2-C_6)alkenyl-, -(C_0-C_6)alkyl-C(=O)NR^{10}-(C_3-C_7)cycloalkyl-, -(C_0-C_6)-alkyl-C(=O)NR^{10}-(C_4-C_{10})alkylcycloalkyl-, -(C_0-C_6)alkyl-S-(C_1-C_6)alkyl-, -(C_0-C_6)-alkyl-S-(C_2-C_6)alkynyl-, -(C_0-C_6)alkyl-S-(C_2-C_6)alkenyl-, -(C_0-C_6)alkyl-S-(C_3-C_7)-cycloalkyl-, -(C_0-C_6)alkyl-S-(C_4-C_{10})alkylcycloalkyl-, -(C_0-C_6)alkyl-S(O)-(C_1-C_6)alkyl-, -(C_0-C_6)alkyl-O-(C_2-C_6)alkynyl-, -(C_0-C_6)alkyl-S(O)-(C_2-C_6)alkenyl-, -(C_0-C_6)alkyl-S(O)-(C_3-C_7)cycloalkyl-, -(C_0-C_6)alkyl-S(O)-(C_4-C_{10})alkylcycloalkyl-, -(C_0-C_6)alkyl-S(O)$_2$-(C_1-C_6)alkyl-, -(C_0-C_6)alkyl-S(O)$_2$-(C_2-C_6)alkynyl-, -(C_0-C_6)alkyl-S(O)$_2$-(C_2-C_6)alkenyl-, -(C_0-C_6)alkyl-S(O)$_2$-(C_3-C_7)cycloalkyl-, -(C_0-C_6)alkyl-S(O)$_2$-(C_4-C_{10})alkylcycloalkyl-, -(C_0-C_6)alkyl-S(O)$_2$$NR^{10}$-($C_1$-$C_6$)alkyl-, -($C_0$-$C_6$)alkyl-S(O)$_2$$NR^{10}$-($C_2$-$C_6$)alkynyl-, -($C_0$-$C_6$)alkyl-S(O)$_2$$NR^{10}$-($C_2$-$C_6$)alkenyl-, -($C_0$-$C_6$)alkyl-S(O)$_2$$NR^{10}$-($C_3$-$C_7$)cycloalkyl-, -($C_0$-$C_6$)alkyl-S(O)$_2$$NR^{10}$-($C_4$-$C_{10}$)alkylcycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$-($C_1$-$C_6$)alkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$-($C_2$-$C_6$)alkynyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$-($C_2$-$C_6$)alkenyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$-($C_3$-$C_7$)cycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$-($C_4$-$C_{10}$)alkylcycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=O)-($C_1$-$C_6$)alkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=O)-($C_2$-$C_6$)alkynyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=O)-($C_2$-$C_6$)alkenyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=O)-($C_3$-$C_7$)cycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=O)-($C_4$-$C_{10}$)alkyl-cycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=O)$NR^{11}$-($C_1$-$C_6$)alkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=O)-$NR^{11}$-($C_2$-$C_6$)alkynyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=O)$NR^{11}$-($C_2$-$C_6$)alkenyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=O)$NR^{11}$-($C_3$-$C_7$)cycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=O)$NR^{11}$-($C_4$-$C_{10}$)-alkylcycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$S(O)$_2$-($C_1$-$C_6$)alkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$S(O)$_2$-($C_2$-$C_6$)alkynyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$S(O)$_2$-($C_2$-$C_6$)alkenyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$S(O)$_2$-($C_3$-$C_7$)cycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$S(O)$_2$-($C_4$-$C_{10}$)alkylcycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=S)$NR^{11}$-($C_1$-$C_6$)alkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}$C(=S)$NR^{11}$-($C_2$-$C_6$)alkynyl-, -($C_0$-

C_6)alkyl-$NR^{10}C(=S)NR^{11}$-(C_2-C_6)alkenyl-, -(C_0-C_6)alkyl-$NR^{10}C(=S)NR^{11}$-(C_3-C_7)-cycloalkyl-, -(C_0-C_6)alkyl-$NR^{10}C(=S)NR^{11}$-(C_4-C_{10})alkylcycloalkyl-, -(C_0-C_6)alkyl-OC(=O)-(C_1-C_6)alkyl-, -(C_0-C_6)alkyl-OC(=O)-(C_2-C_6)alkynyl-, -(C_0-C_6)alkyl-OC(=O)-(C_2-C_6)alkenyl-, -(C_0-C_6)alkyl-OC(=O)-(C_4-C_{10})alkylcycloalkyl-, -(C_0-C_6)alkyl-OC(=O)-(C_3-C_7)cycloalkyl-, -(C_0-C_6)alkyl-OC(=O)NR^{10}-(C_1-C_6)alkyl-, -(C_0-C_6)alkyl-OC(=O)NR^{10}-(C_2-C_6)alkynyl-, -(C_0-C_6)alkyl-OC(=O)NR^{10}-(C_2-C_6)alkenyl-, -(C_0-C_6)-alkyl-OC(=O)NR^{10}-(C_4-C_{10})alkylcycloalkyl-, -(C_0-C_6)alkyl-OC(=O)NR^{10}-(C_3-C_7)-cycloalkyl-, -(C_0-C_6)alkyl-$NR^{10}C(=O)O$-(C_1-C_6)alkyl-, -(C_0-C_6)alkyl-$NR^{10}C(=O)O$-(C_2-C_6)alkynyl-, -(C_0-C_6)alkyl-$NR^{10}C(=O)O$-(C_2-C_6)alkenyl-, -(C_0-C_6)alkyl-$NR^{10}C(=O)O$-(C_3-C_7)cycloalkyl-, -(C_0-C_6)alkyl-$NR^{10}C(=O)O$-(C_4-C_{10})alkylcycloalkyl-, -(C_0-C_6)alkyl-$NR^{10}C(=NR^{11})NR^{12}$-($C_1$-$C_6$)alkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}C(=NR^{11})NR^{12}$-($C_2$-$C_6$)alkynyl-, -($C_0$-$C_6$)alkyl-$NR^{10}C(=NR^{11})NR^{12}$-($C_2$-$C_6$)-alkenyl-, -($C_0$-$C_6$)alkyl-$NR^{10}C(=NR^{11})NR^{12}$-($C_3$-$C_7$)cycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}C(=NR^{11})NR^{12}$-($C_4$-$C_{10}$)alkylcycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}C(=NR^{11})$-($C_1$-$C_6$)alkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}C(=NR^{11})$-($C_2$-$C_6$)alkynyl-, -($C_0$-$C_6$)alkyl-$NR^{10}C(=NR^{11})$-($C_2$-$C_6$)-alkenyl-, -($C_0$-$C_6$)alkyl-$NR^{10}C(=NR^{11})$-($C_3$-$C_7$)cycloalkyl-, -($C_0$-$C_6$)alkyl-$NR^{10}C(=NR^{11})$-($C_4$-$C_{10}$)alkylcycloalkyl-, -($C_0$-$C_6$)alkyl-$C(=NR^{10})NR^{11}$-($C_1$-$C_6$)alkyl-, -($C_0$-$C_6$)alkyl-$C(=NR^{10})NR^{11}$-($C_2$-$C_6$)alkynyl-, -($C_0$-$C_6$)alkyl-$C(=NR^{10})NR^{11}$-($C_2$-$C_6$)-alkenyl-, -($C_0$-$C_6$)alkyl-$C(=NR^{10})NR^{11}$-($C_3$-$C_7$)cycloalkyl- and -($C_0$-$C_6$)alkyl-$C(=NR^{10})NR^{11}$-($C_4$-$C_{10}$)alkylcycloalkyl-;

(R^2 and R^3) or (R^4 and R^5) taken together may form an optionally substituted 3 to 10 membered ring selected from the group of aryl, heteroaryl, heterocyclic and cycloalkyl;

M_1 and M_2 are each independently selected from the group of hydrogen, -CN, -OH, $-NO_2$, $-CF_3$, $-NH_2$, -SH, $-C(=NR^{14})NR^{15}R^{16}$, $-C(=O)R^{14}$, $-C(=NR^{14})R^{15}$, $-C(=O)OR^{14}$, $-C(=O)NR^{14}R^{15}$, $-SR^{14}$, $-S(O)R^{14}$, $-S(O)_2R^{14}$, $-NR^{14}R^{15}$, $-NR^{14}C(=O)R^{15}$, $-NR^{14}C(=NR^{15})R^{16}$, $-NR^{14}C(=NR^{15})NR^{16}R^{17}$, $-NR^{14}C(=O)OR^{15}$, $-NR^{14}C(=O)NR^{15}R^{16}$, $-NR^{14}S(O)_2R^{15}$, $-C(=S)NR^{14}R^{15}$, $-OC(=O)R^{14}$, $-OC(=O)NR^{14}R^{15}$, $-OR^{14}$, $-S(O)_2NR^{14}R^{15}$, and an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_8)cycloalkyl, -(C_3-C_8)cycloalkenyl and an optionally substituted 3 to 10 membered ring selected from the group of aryl, heteroaryl, heterocyclic and cycloalkyl ;

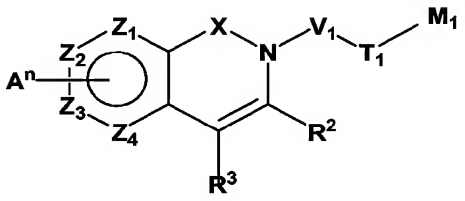
R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17} are each independently hydrogen or an optionally substituted radical selected from the group of -(C_1-C_6)alkylhalo, -(C_1-C_6)-alkyl, -(C_1-C_6)alkylcyano, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_4-C_{10})alkylcycloalkyl, heteroaryl, -(C_1-C_6)alkylheteroaryl, aryl, -(C_1-C_6)alkylaryl, -(C_2-C_6)alkynyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkynyl-heteroaryl, -(C_2-C_6)alkynyl-aryl, -(C_2-C_6)alkenyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkenyl-heteroaryl and -(C_2-C_6)alkenyl-aryl;

R^7, R^8 and R^9 may be taken together to form an optionally substituted 3 to 10 membered non-aromatic heterocyclic ring or an optionally substituted 5 to 10 membered aromatic heterocyclic ring;

R^{10}, R^{11}, R^{12} and R^{13} may be taken together to form an optionally substituted 3 to 10 membered non-aromatic heterocyclic ring or an optionally substituted 5 to 10 membered aromatic heterocyclic ring; and

R^{14}, R^{15}, R^{16} and R^{17} may be taken together to form an optionally substituted 3 to 10 membered non-aromatic heterocyclic ring or an optionally substituted 5 to 10 membered aromatic heterocyclic ring.

In a first preferred aspect of Formula (I), the invention concerns a compound according to Formula (II)



(II)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

X is selected from C(=O) and $S(O)_2$;

Z_1, Z_2, Z_3 and Z_4 are each independently, selected from the group of a covalent bond, C, S, N and O, representing a 5 or 6 membered heteroaryl or aryl ring which may further be substituted by 1 to 4 radicals A^n ;

A^n radicals are each independently selected from the group of hydrogen, halogen, -CN, -OH, $-NO_2$, $-CF_3$, -SH, $-NH_2$, and an optionally substituted radical selected from the group of $-(C_1-C_6)$alkyl, $-(C_1-C_6)$alkylhalo, $-(C_2-C_6)$alkynyl, $-(C_2-C_6)$alkenyl, $-(C_3-C_7)$-cycloalkyl, $-(C_1-C_6)$alkylcyano, $-O-(C_1-C_6)$alkyl, $-O-(C_1-C_6)$alkylhalo, $-O-(C_1-C_6)$-alkylcyano, $-O-(C_3-C_6)$alkynyl, $-O-(C_3-C_7)$cycloalkyl, $-O-(C_2-C_6)$alkenyl, $-O-(C_2-C_6)$-alkyl-OR^{18}, $-O-(C_1-C_6)$alkyl-heteroaryl, $-O-(C_0-C_6)$alkylaryl, $-(C_0-C_6)$alkyl-OR^{18}, $-(C_3-C_7)$cycloalkyl-(C_1-C_6)alkyl, $-O-(C_3-C_7)$cycloalkyl-(C_1-C_6)alkyl, -O-heteroaryl, heteroaryl, $-(C_1-C_6)$alkyl-heteroaryl, aryl, -O-aryl, $-(C_1-C_6)$alkylaryl, $-(C_1-C_6)$alkylhalo-OR^{18}, $-(C_3-C_6)$alkynyl-OR^{18}, $-(C_3-C_6)$alkenyl-OR^{18}, $-(C_0-C_6)$alkyl-S-R^{18}, $-O-(C_2-C_6)$-alkyl-S-R^{18}, $-(C_1-C_6)$alkyl-S(=O)-R^{18}, $-O-(C_1-C_6)$alkyl-S(=O)-R^{18}, $-(C_0-C_6)$alkyl-$S(=O)_2$-R^{18}, $-O-(C_1-C_6)$alkyl-$S(=O)_2$-R^{18}, $-(C_0-C_6)$alkyl-$NR^{18}R^{19}$, $-O-(C_2-C_6)$alkyl-$NR^{18}R^{19}$, $-(C_0-C_6)$alkyl-$S(=O)_2NR^{18}R^{19}$, $-(C_0-C_6)$alkyl-NR^{18}-$S(=O)_2R^{19}$, $-O-(C_1-C_6)$-alkyl-$S(=O)_2NR^{18}R^{19}$, $-O-(C_1-C_6)$alkyl-NR^{18}-$S(=O)_2R^{19}$, $-(C_0-C_6)$alkyl-C(=O)-$NR^{18}R^{19}$, $-(C_0-C_6)$alkyl-NR^{18}C(=O)-R^{19}, $-O-(C_1-C_6)$alkyl-C(=O)-$NR^{18}R^{19}$, $-O-(C_1-C_6)$alkyl-NR^{18}C(=O)-R^{19}, $-(C_0-C_6)$alkyl-OC(=O)-R^{18}, $-(C_0-C_6)$alkyl-C(=O)-OR^{18}, $-O-(C_1-C_6)$-alkyl-OC(=O)-R^{18}, $-O-(C_1-C_6)$alkyl-C(=O)-OR^{18}, $-(C_0-C_6)$alkyl-C(=O)-R^{18}, $-O-(C_1-C_6)$alkyl-C(=O)-R^{18}, $-(C_0-C_6)$alkyl-NR^{18}-C(=O)-OR^{19}, $-(C_0-C_6)$alkyl-O-C(=O)-$NR^{18}R^{19}$, $-(C_0-C_6)$alkyl-NR^{18}-C(=NR^{19})-$NR^{20}R^{21}$, $-(C_0-C_6)$alkyl-NR^{18}-C(=O)-$NR^{19}R^{20}$, $-(C_0-C_6)$alkyl-NR^{18}-C(=S)-$NR^{19}R^{20}$ and a $-V_2-T_2-M_2$ radical;

n is an integer ranging from 1 to 4;

R^{18}, R^{19}, R^{20} and R^{21} are each independently hydrogen or an optionally substituted radical selected from the group of $-(C_1-C_6)$alkylhalo, $-(C_1-C_6)$alkyl, $-(C_1-C_6)$alkylcyano, $-(C_2-C_6)$alkynyl, $-(C_2-C_6)$alkenyl, $-(C_3-C_7)$cycloalkyl, $-(C_4-C_{10})$alkylcycloalkyl, heteroaryl, $-(C_1-C_6)$alkylheteroaryl, aryl, $-(C_1-C_6)$alkylaryl, $-(C_2-C_6)$alkynyl-(C_3-C_7)-cycloalkyl, $-(C_2-C_6)$alkynyl-heteroaryl, $-(C_2-C_6)$alkynyl-aryl, $-(C_2-C_6)$alkenyl-(C_3-C_7)-cycloalkyl, $-(C_2-C_6)$alkenyl-heteroaryl and $-(C_2-C_6)$alkenyl-aryl; and

R^{18}, R^{19}, R^{20} and R^{21} may be taken together to form an optionally substituted 3 to 10 membered non-aromatic heterocyclic ring or an optionally substituted 5 to 10 membered aromatic heterocyclic ring.

Preferred structures according to Formula (II) are indicated in Figure A below.

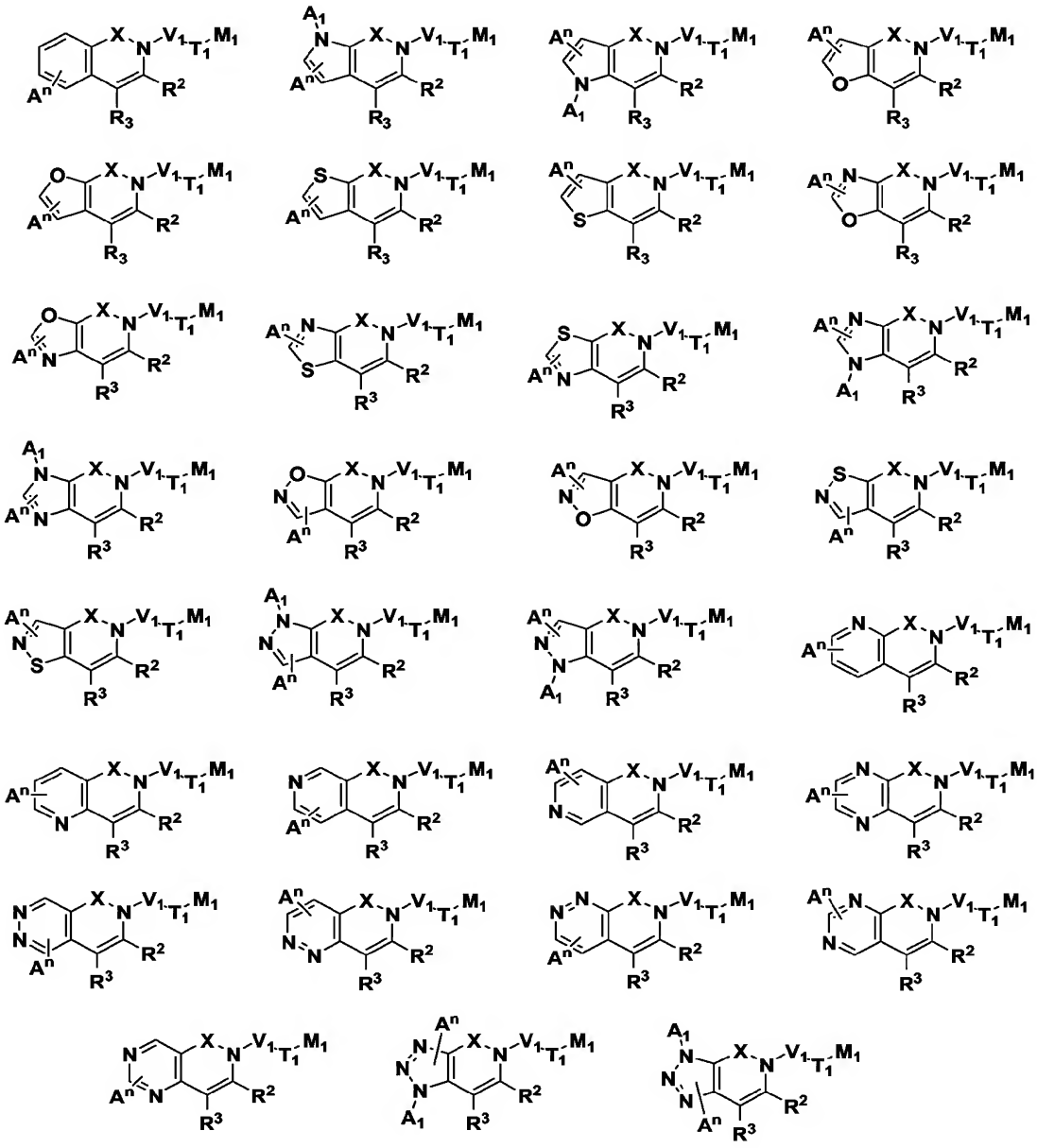
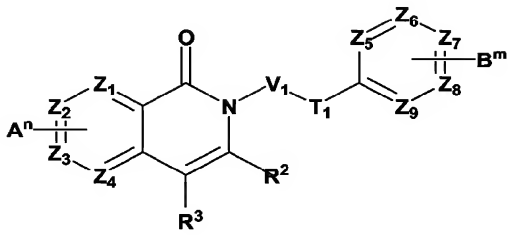


Figure A

In a more preferred aspect of Formula (II), the invention provides a compound according to Formula (II-a),



(II-a)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

Z_5, Z_6, Z_7, Z_8 and Z_9 are each independently selected from the group of a covalent bond, C, S, N and O, representing a 5 or 6 membered heteroaryl or aryl ring which may optionally be substituted by 1 to 5 radicals B^m ;

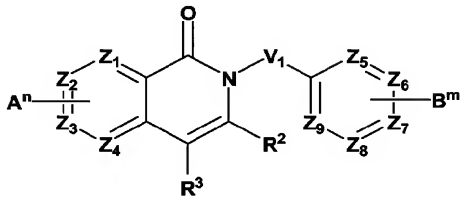
B^m radicals are each independently selected from the group of hydrogen, halogen, -CN, -OH, $-NO_2$, $-CF_3$, -SH, $-NH_2$, and an optionally substituted radical selected from the group of $-(C_1-C_6)$alkyl, $-(C_1-C_6)$alkylhalo, $-(C_2-C_6)$alkynyl, $-(C_2-C_6)$alkenyl, $-(C_3-C_7)$-cycloalkyl, $-(C_1-C_6)$alkylcyano, $-O-(C_1-C_6)$alkyl, $-O-(C_1-C_6)$alkylhalo, $-O-(C_1-C_6)$-alkylcyano, $-O-(C_3-C_6)$alkynyl, $-O-(C_3-C_7)$cycloalkyl, $-O-(C_2-C_6)$alkenyl, $-O-(C_2-C_6)$-alkyl-OR^{22}, $-O-(C_1-C_6)$alkyl-heteroaryl, $-O-(C_0-C_6)$alkylaryl, $-(C_0-C_6)$alkyl-OR^{22}, $-(C_3-C_7)$cycloalkyl-(C_1-C_6)alkyl, $-O-(C_3-C_7)$cycloalkyl-(C_1-C_6)alkyl, -O-heteroaryl, heteroaryl, $-(C_1-C_6)$alkyl-heteroaryl, aryl, -O-aryl, $-(C_1-C_6)$alkylaryl, $-(C_1-C_6)$alkylhalo-OR^{22}, $-(C_3-C_6)$alkynyl-OR^{22}, $-(C_3-C_6)$alkenyl-OR^{22}, $-(C_0-C_6)$alkyl-S-R^{22}, $-O-(C_2-C_6)$-alkyl-S-R^{22}, $-(C_1-C_6)$alkyl-S(=O)-R^{22}, $-O-(C_1-C_6)$alkyl-S(=O)-R^{22}, $-(C_0-C_6)$alkyl-$S(=O)_2$-R^{22}, $-O-(C_1-C_6)$alkyl-$S(=O)_2$-R^{22}, $-(C_0-C_6)$alkyl-$NR^{22}R^{23}$, $-O-(C_2-C_6)$alkyl-$NR^{22}R^{23}$, $-(C_0-C_6)$alkyl-$S(=O)_2NR^{22}R^{23}$, $-(C_0-C_6)$alkyl-NR^{22}-$S(=O)_2R^{23}$, $-O-(C_1-C_6)$-alkyl-$S(=O)_2NR^{22}R^{23}$, $-O-(C_1-C_6)$alkyl-NR^{22}-$S(=O)_2R^{23}$, $-(C_0-C_6)$alkyl-C(=O)-$NR^{22}R^{23}$, $-(C_0-C_6)$alkyl-NR^{22}C(=O)-R^{23}, $-O-(C_1-C_6)$alkyl-C(=O)-$NR^{22}R^{23}$, $-O-(C_1-C_6)$alkyl-NR^{22}C(=O)-R^{23}, $-(C_0-C_6)$alkyl-OC(=O)-R^{22}, $-(C_0-C_6)$alkyl-C(=O)-OR^{22}, $-O-(C_1-C_6)$-alkyl-OC(=O)-R^{22}, $-O-(C_1-C_6)$alkyl-C(=O)-OR^{22}, $-(C_0-C_6)$alkyl-C(=O)-R^{22}, $-O-(C_1-C_6)$alkyl-C(=O)-R^{22}, $-(C_0-C_6)$alkyl-NR^{22}-C(=O)-OR^{23}, $-(C_0-C_6)$alkyl-O-C(=O)-$NR^{22}R^{23}$, $-(C_0-C_6)$alkyl-NR^{22}-C(=NR^{23})-$NR^{24}R^{25}$, $-(C_0-C_6)$alkyl-NR^{22}-C(=O)-$NR^{23}R^{24}$ and $-(C_0-C_6)$alkyl-NR^{22}-C(=S)-$NR^{23}R^{24}$;

m is an integer ranging from 1 to 5;

R^{22}, R^{23}, R^{24} and R^{25} are each independently selected from hydrogen or an optionally substituted radical selected from the group of -(C_1-C_6)alkylhalo, -(C_1-C_6)alkyl, -(C_1-C_6)alkylcyano, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_4-C_{10})-alkylcycloalkyl, heteroaryl, -(C_1-C_6)alkylheteroaryl, aryl, -(C_1-C_6)alkylaryl, -(C_2-C_6)-alkynyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkynyl-heteroaryl, -(C_2-C_6)alkynyl-aryl, -(C_2-C_6)-alkenyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkenyl-heteroaryl and -(C_2-C_6)alkenyl-aryl ; and

R^{22}, R^{23}, R^{24} and R^{25} may be taken together to form an optionally substituted 3 to 10 membered non-aromatic heterocyclic ring or an optionally substituted 5 to 10 membered aromatic heterocyclic ring.

In a further preferred aspect of Formula (II-a), the invention provides a compound of Formula (II-b),



(II-b)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

V_1 is an optionally substituted radical selected from the group of -(C_1-C_6)alkyl-, -(C_2-C_6)alkynyl-, -(C_2-C_6)alkenyl-, -(C_3-C_7)cycloalkyl-, -(C_3-C_8)cycloalkenyl-, -(C_1-C_6)-alkylhalo-, -(C_1-C_6)alkyl-C(=O)-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-C(=O)-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-C(=O)-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-C(=O)-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-C(=O)-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-C(=O)O-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-C(=O)O-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-C(=O)O-(C_2-C_6)alkenyl-, -(C_1-C_6)-alkyl-C(=O)O-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-C(=O)O-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-O-

$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-O-$(C_2\text{-}C_6)$alkynyl-, -$(C_1\text{-}C_6)$alkyl-O-$(C_2\text{-}C_6)$alkenyl-, -$(C_1\text{-}C_6)$alkyl-O-$(C_3\text{-}C_7)$cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-O-$(C_4\text{-}C_{10})$alkylcycloalkyl-, -$(C_1\text{-}C_6)$-alkyl-S-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-S-$(C_2\text{-}C_6)$alkynyl-, -$(C_1\text{-}C_6)$alkyl-S-$(C_2\text{-}C_6)$-alkenyl-, -$(C_1\text{-}C_6)$alkyl-S-$(C_3\text{-}C_7)$cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-S-$(C_4\text{-}C_{10})$alkylcycloalkyl-, -$(C_1\text{-}C_6)$alkyl-S(O)-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-S(O)-$(C_2\text{-}C_6)$alkynyl-, -$(C_1\text{-}C_6)$alkyl-S(O)-$(C_2\text{-}C_6)$alkenyl-, -$(C_1\text{-}C_6)$alkyl-S(O)-$(C_3\text{-}C_7)$cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-S(O)-$(C_4\text{-}C_{10})$alkylcycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$S(O)_2$-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-$S(O)_2$-$(C_2\text{-}C_6)$-alkynyl-, -$(C_1\text{-}C_6)$alkyl-$S(O)_2$-$(C_2\text{-}C_6)$alkenyl-, -$(C_1\text{-}C_6)$alkyl-$S(O)_2$-$(C_3\text{-}C_7)$cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$S(O)_2$-$(C_4\text{-}C_{10})$alkylcycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$S(O)_2NR^7$-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-$S(O)_2NR^7$-$(C_2\text{-}C_6)$alkynyl-, -$(C_1\text{-}C_6)$alkyl-$S(O)_2NR^7$-$(C_2\text{-}C_6)$alkenyl-, -$(C_1\text{-}C_6)$alkyl-$S(O)_2NR^7$-$(C_3\text{-}C_7)$cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$S(O)_2NR^7$-$(C_4\text{-}C_{10})$alkyl-cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-NR^7-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-NR^7-$(C_2\text{-}C_6)$alkynyl-, -$(C_1\text{-}C_6)$alkyl-NR^7-$(C_2\text{-}C_6)$alkenyl-, -$(C_1\text{-}C_6)$alkyl-NR^7-$(C_3\text{-}C_7)$cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-NR^7-$(C_4\text{-}C_{10})$alkylcycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)$-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)$-$(C_2\text{-}C_6)$alkynyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)$-$(C_2\text{-}C_6)$alkenyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)$-$(C_3\text{-}C_7)$cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)$-$(C_4\text{-}C_{10})$alkylcycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)NR^8$-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)NR^8$-$(C_2\text{-}C_6)$-alkynyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)NR^8$-$(C_2\text{-}C_6)$alkenyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)NR^8$-$(C_3\text{-}C_7)$cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)NR^8$-$(C_4\text{-}C_{10})$alkylcycloalkyl-, -$(C_1\text{-}C_6)$-alkyl-$NR^7S(O)_2$-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7S(O)_2$-$(C_2\text{-}C_6)$alkynyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7S(O)_2$-$(C_2\text{-}C_6)$alkenyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7S(O)_2$-$(C_3\text{-}C_7)$cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7S(O)_2$-$(C_4\text{-}C_{10})$alkylcycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=S)NR^8$-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=S)NR^8$-$(C_2\text{-}C_6)$alkynyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=S)NR^8$-$(C_2\text{-}C_6)$alkenyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=S)NR^8$-$(C_3\text{-}C_7)$cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=S)NR^8$-$(C_4\text{-}C_{10})$alkylcycloalkyl-, -$(C_1\text{-}C_6)$alkyl-OC(=O)-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-OC(=O)-$(C_2\text{-}C_6)$alkynyl-, -$(C_1\text{-}C_6)$alkyl-OC(=O)-$(C_2\text{-}C_6)$alkenyl-, -$(C_1\text{-}C_6)$alkyl-OC(=O)-$(C_3\text{-}C_7)$-cycloalkyl-, -$(C_1\text{-}C_6)$alkyl-OC(=O)-$(C_4\text{-}C_{10})$alkylcycloalkyl-, -$(C_1\text{-}C_6)$alkyl-OC(=O)NR^7-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-OC(=O)NR^7-$(C_2\text{-}C_6)$alkynyl-, -$(C_1\text{-}C_6)$alkyl-OC(=O)NR^7-$(C_2\text{-}C_6)$alkenyl-, -$(C_1\text{-}C_6)$alkyl-OC(=O)NR^7-$(C_3\text{-}C_7)$cycloalkyl-, -$(C_1\text{-}C_6)$-alkyl-OC(=O)NR^7-$(C_4\text{-}C_{10})$alkylcycloalkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)O$-$(C_0\text{-}C_6)$alkyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)O$-$(C_2\text{-}C_6)$alkynyl-, -$(C_1\text{-}C_6)$alkyl-$NR^7C(=O)O$-$(C_2\text{-}C_6)$-

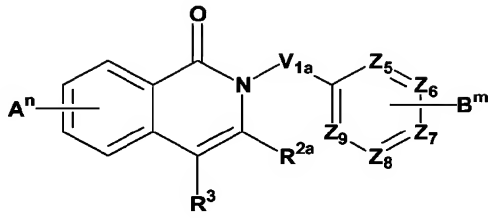
alkenyl-, -(C_1-C_6)alkyl-NR^7C(=O)O-(C_3-C_7)cycloalkyl- and -(C_1-C_6)alkyl-NR^7C(=O)O-(C_4-C_{10})alkylcycloalkyl-;

R^2 is selected from the group of hydrogen, halogen, -CN, -CF_3, and an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_2-C_6)alkenyl, -(C_2-C_6)-alkynyl, -(C_1-C_6)alkylhalo, -(C_3-C_7)cycloalkyl, -(C_1-C_6)alkylcyano, -O-(C_1-C_6)alkyl, -O-(C_1-C_6)alkylhalo, -O-(C_1-C_6)alkylcyano, -O-(C_3-C_6)alkynyl, -O-(C_3-C_7)cycloalkyl, -O-(C_2-C_6)alkyl-OR^{26}, -O-(C_1-C_6)alkyl-heteroaryl, -O-(C_0-C_6)alkylaryl, -(C_0-C_6)alkyl-OR^{26}, -O-heteroaryl, -heteroaryl, -(C_1-C_6)alkyl-heteroaryl, -aryl, -O-aryl, -(C_1-C_6)-alkylaryl, -(C_1-C_6)alkylhalo-OR^{26}, -(C_0-C_6)alkyl-SR^{26}, -(C_0-C_6)alkyl-S(=O)$_2$-R^{26}, -(C_0-C_6)alkyl-$NR^{26}R^{27}$, -O-(C_2-C_6)alkyl-$NR^{26}R^{27}$, -(C_0-C_6)alkyl-S(=O)$_2$$NR^{26}R^{27}$, -($C_0$-$C_6$)-alkyl-$NR^{26}$-S(=O)$_2$$R^{27}$, -($C_0$-$C_6$)alkyl-C(=O)-$NR^{26}R^{27}$, -($C_0$-$C_6$)alkyl-$NR^{26}$C(=O)-$R^{27}$, -O-($C_1$-$C_6$)alkylC(=O)-$NR^{26}R^{27}$, -O-($C_1$-$C_6$)alkyl-$NR^{26}$C(=O)-$R^{27}$ and -(C_0-C_6)alkyl-C(=O)-R^{26};

R^{26} and R^{27} are each independently hydrogen or an optionally substituted radical selected from the group of -(C_1-C_6)alkylhalo, -(C_1-C_6)alkylcyano, -(C_0-C_6)alkyl, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_4-C_{10})alkylcycloalkyl, heteroaryl, -(C_1-C_6)alkylheteroaryl, aryl, -(C_1-C_6)alkylaryl, -(C_2-C_6)alkynyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkynyl-heteroaryl, -(C_2-C_6)alkynyl-aryl, -(C_2-C_6)alkenyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkenyl-heteroaryl and -(C_2-C_6)alkenyl-aryl; and

R^{26} and R^{27} may be taken together to form an optionally substituted 3 to 10 membered non-aromatic heterocyclic ring or an optionally substituted 5 to 10 membered aromatic heterocyclic ring.

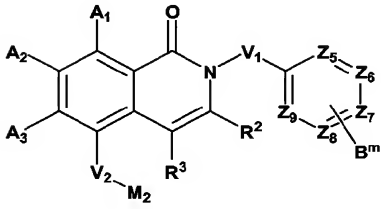
In a further preferred aspect of Formula (II-b) the invention provides a compound of Formula (II-c),



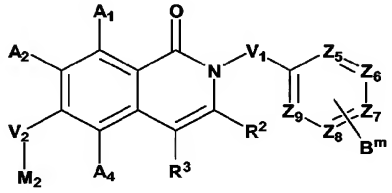
(II-c)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof.

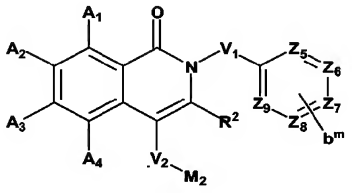
In a further preferred aspect of Formula (II-c) the invention provides a compound according to any one of Formulas (II-c1), (II-c2) and (II-c3),



(II-c1)



(II-c2)



(II-c2)

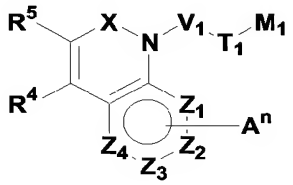
a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

Z_5 ,Z_6 ,Z_7, Z_8 and Z_9 are selected from C or N, provided that at least 2 carbons are present and that a free position may further be substituted by 1 to 5 radicals B^m ; and

R^2, R^3, A^1, A^2, A^3 and A^4 are each independently selected from the group of hydrogen, halogen, -CN, -CF_3, -OCF_3, and an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_3-C_8)-cycloalkenyl, -(C_1-C_6)alkylhalo, -(C_0-C_3)alkyl-O-(C_1-C_6)alkyl, -(C_0-C_3)alkyl-O-(C_2-C_6)alkynyl, -(C_0-C_3)alkyl-O-(C_2-C_6)alkenyl, -(C_0-C_3)alkyl-O-(C_3-C_7)cycloalkyl, -(C_0-C_3)alkyl-O-(C_4-C_{10})alkylcycloalkyl, -(C_0-C_3)alkyl-O-(C_1-C_6)alkylhalo, -S-(C_1-C_6)alkyl, -S-(C_2-C_6)alkynyl, -S-(C_2-C_6)alkenyl, -S-(C_3-C_7)cycloalkyl, -S-(C_4-C_{10})alkyl-

cycloalkyl, -(C_0-C_3)alkyl-$NR^{18}R^{19}$, -(C_0-C_3)alkyl-$S(O)_2NR^{18}R^{19}$, -(C_0-C_3)alkyl-$NR^{18}S(O)_2R^{19}$, -(C_0-C_3)alkyl-C(=O)R^{18}, -(C_0-C_3)alkyl-C(=O)OR^{18}, -(C_0-C_3)alkyl-C(=O)$NR^{18}R^{19}$, -(C_0-C_3)alkyl-NR^{18}C(=O)R^{19}, -O-(C_0-C_3)alkyl-$S(O)_2NR^{18}R^{19}$, -O-(C_0-C_3)alkyl-$NR^{18}S(O)_2R^{19}$, -O-(C_0-C_3)alkyl-C(=O)R^{18}, -O-(C_0-C_3)alkyl-C(=O)OR^{18}, -O-(C_0-C_3)alkyl-C(=O)$NR^{18}R^{19}$ and -O-(C_0-C_3)alkyl- NR^{18}C(=O)R^{19}.

In a second preferred aspect of Formula (I), the invention provides a compound according to Formula (III),



(III)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

X is selected from C(=O) and $S(O)_2$;

Z_1, Z_2, Z_3 and Z_4 are each independently, selected from the group of a covalent bond, C, S, N and O, representing a 5 or 6 membered heteroaryl or aryl ring which may further be substituted by 1 to 4 radicals A^n ;

A^n radicals are each independently selected from the group of hydrogen, halogen, -CN, -OH, $-NO_2$, $-CF_3$, -SH, $-NH_2$, and an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_1-C_6)alkylhalo, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)-cycloalkyl, -(C_1-C_6)alkylcyano, -O-(C_1-C_6)alkyl, -O-(C_1-C_6)alkylhalo, -O-(C_1-C_6)-alkylcyano, -O-(C_3-C_6)alkynyl, -O-(C_3-C_7)cycloalkyl, -O-(C_2-C_6)alkenyl, -O-(C_2-C_6)-alkyl-OR^{18}, -O-(C_1-C_6)alkyl-heteroaryl, -O-(C_0-C_6)alkylaryl, -(C_0-C_6)alkyl-OR^{18}, -(C_3-C_7)cycloalkyl-(C_1-C_6)alkyl, -O-(C_3-C_7)cycloalkyl-(C_1-C_6)alkyl, -O-heteroaryl, heteroaryl, -(C_1-C_6)alkyl-heteroaryl, aryl, -O-aryl, -(C_1-C_6)alkylaryl, -(C_1-C_6)alkylhalo-OR^{18}, -(C_3-C_6)alkynyl-OR^{18}, -(C_3-C_6)alkenyl-OR^{18}, -(C_0-C_6)alkyl-SR^{18}, -O-(C_2-C_6)-alkyl-SR^{18}, -(C_1-C_6)alkyl-S(=O)R^{18}, -O-(C_1-C_6)alkyl-S(=O)R^{18}, -(C_0-C_6)alkyl-$S(=O)_2R^{18}$, -O-(C_1-C_6)alkyl-$S(=O)_2R^{18}$, -(C_0-C_6)alkyl-$NR^{18}R^{19}$, -O-(C_2-C_6)alkyl-$NR^{18}R^{19}$, -(C_0-C_6)alkyl-$S(=O)_2NR^{18}R^{19}$, -(C_0-C_6)alkyl-NR^{18}-$S(=O)_2R^{19}$, -O-(C_1-

C_6)alkyl-$S(=O)_2NR^{18}R^{19}$, -O-(C_1-C_6)alkyl-NR^{18}-$S(=O)_2R^{19}$, -(C_0-C_6)alkyl-$C(=O)$-$NR^{18}R^{19}$, -(C_0-C_6)alkyl-$NR^{18}C(=O)$-R^{19}, -O-(C_1-C_6)alkyl$C(=O)$-$NR^{18}R^{19}$, -O-(C_1-C_6)-alkyl-$NR^{18}C(=O)$-R^{19}, -(C_0-C_6)alkyl-$OC(=O)$-R^{19}, -(C_0-C_6)alkyl-$C(=O)$-OR^{18}, -O-(C_1-C_6)alkyl-$OC(=O)$-R^{18}, -O-(C_1-C_6)alkyl-$C(=O)$-OR^{18}, -(C_0-C_6)alkyl-$C(=O)$-R^{18}, -O-(C_1-C_6)alkyl-$C(=O)$-R^{18}, -(C_0-C_6)alkyl-NR^{18}-$C(=O)$-OR^{19}, -(C_0-C_6)alkyl-O-$C(=O)$-$NR^{18}R^{19}$, -(C_0-C_6)alkyl-NR^{18}-$C(=NR^{19})$-$NR^{20}R^{21}$, -(C_0-C_6)alkyl-NR^{18}-$C(=O)$-$NR^{19}R^{20}$, -(C_0-C_6)alkyl-NR^{18}-$C(=S)$-$NR^{19}R^{20}$, and a -V_2-T_2-M_2 radical;

n is an integer ranging from 1 to 4;

R^{18}, R^{19}, R^{20} and R^{21} are each independently hydrogen or an optionally substituted radical selected from the group of -(C_1-C_6)alkylhalo, -(C_1-C_6)alkyl, -(C_1-C_6)alkylcyano, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_4-C_{10})alkylcycloalkyl, heteroaryl, -(C_1-C_6)alkylheteroaryl, aryl, -(C_1-C_6)alkylaryl, -(C_2-C_6)alkynyl-(C_3-C_7)-cycloalkyl, -(C_2-C_6)alkynyl-heteroaryl, -(C_2-C_6)alkynyl-aryl, -(C_2-C_6)alkenyl-(C_3-C_7)-cycloalkyl, -(C_2-C_6)alkenyl-heteroaryl and -(C_2-C_6)alkenyl-aryl; and

R^{18}, R^{19}, R^{20} and R^{21} may be taken together to form an optionally substituted 3 to 10 membered non-aromatic heterocyclic ring oran optionally substituted 5 to 10 membered aromatic heterocyclic ring.

Preferred structures from Formula (III) are indicated in Figure B below.

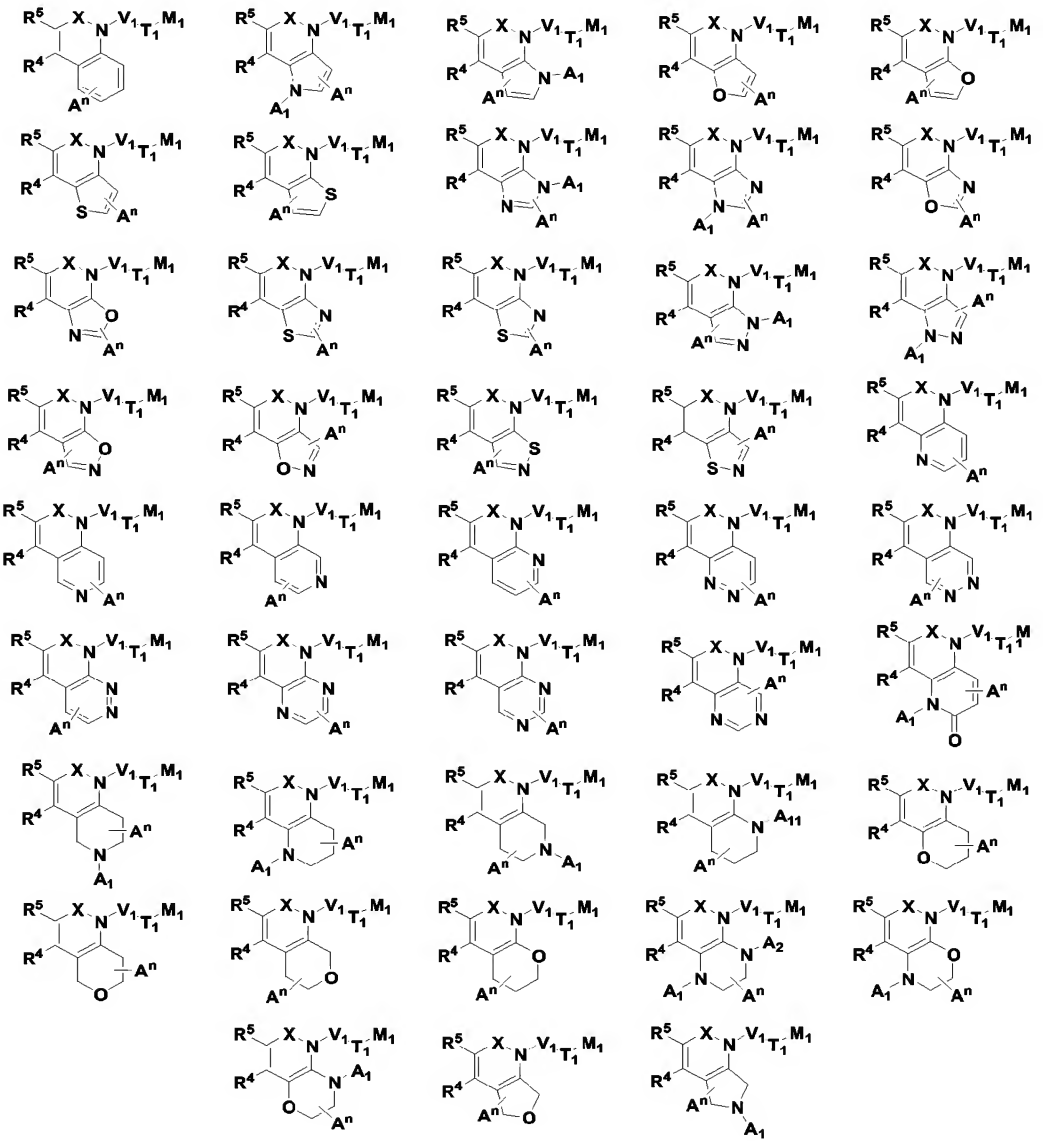
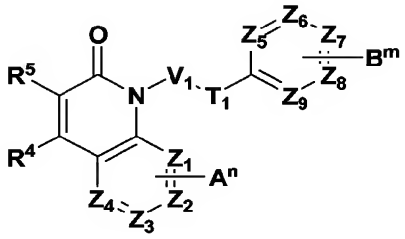


Figure B

In a preferred aspect of Formula (III) the invention provides a compound of Formula (III-a),



(III-a)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

Z_5, Z_6, Z_7, Z_8 and Z_9 are each independently selected from the group of a covalent bond, C, S, N and O, representing a 5 or 6 membered heteroaryl or aryl ring which may optionally be substituted by 1 to 5 radicals B^m ;

B^m radicals are each independently selected from the group of hydrogen, halogen, -CN, -OH, $-NO_2$, $-CF_3$, -SH, $-NH_2$, and an optionally substituted radical selected from the group of $-(C_1-C_6)$alkyl, $-(C_1-C_6)$alkylhalo, $-(C_2-C_6)$alkynyl, $-(C_2-C_6)$alkenyl, $-(C_3-C_7)$-cycloalkyl, $-(C_1-C_6)$alkylcyano, $-O-(C_1-C_6)$alkyl, $-O-(C_1-C_6)$alkylhalo, $-O-(C_1-C_6)$-alkylcyano, $-O-(C_3-C_6)$alkynyl, $-O-(C_3-C_7)$cycloalkyl, $-O-(C_2-C_6)$alkenyl, $-O-(C_2-C_6)$-alkyl-OR^{22}, $-O-(C_1-C_6)$alkyl-heteroaryl, $-O-(C_0-C_6)$alkylaryl, $-(C_0-C_6)$alkyl-OR^{22}, $-(C_3-C_7)$cycloalkyl-(C_1-C_6)alkyl, $-O-(C_3-C_7)$cycloalkyl-(C_1-C_6)alkyl, -O-heteroaryl, heteroaryl, $-(C_1-C_6)$alkyl-heteroaryl, aryl, -O-aryl, $-(C_1-C_6)$alkylaryl, $-(C_1-C_6)$alkylhalo-OR^{22}, $-(C_3-C_6)$alkynyl-OR^{22}, $-(C_3-C_6)$alkenyl-OR^{22}, $-(C_0-C_6)$alkyl-S-R^{22}, $-O-(C_2-C_6)$-alkyl-S-R^{22}, $-(C_1-C_6)$alkyl-S(=O)-R^{22}, $-O-(C_1-C_6)$alkyl-S(=O)-R^{22}, $-(C_0-C_6)$alkyl-$S(=O)_2$-R^{22}, $-O-(C_1-C_6)$alkyl-$S(=O)_2$-R^{22}, $-(C_0-C_6)$alkyl-$NR^{22}R^{23}$, $-O-(C_2-C_6)$alkyl-$NR^{22}R^{23}$, $-(C_0-C_6)$alkyl-$S(=O)_2NR^{22}R^{23}$, $-(C_0-C_6)$alkyl-NR^{22}-$S(=O)_2R^{23}$, $-O-(C_1-C_6)$-alkyl-$S(=O)_2NR^{22}R^{23}$, $-O-(C_1-C_6)$alkyl-NR^{22}-$S(=O)_2R^{23}$, $-(C_0-C_6)$alkyl-C(=O)-$NR^{22}R^{23}$, $-(C_0-C_6)$alkyl-NR^{22}C(=O)-R^{23}, $-O-(C_1-C_6)$alkyl-C(=O)-$NR^{22}R^{23}$, $-O-(C_1-C_6)$alkyl-NR^{22}C(=O)-R^{23}, $-(C_0-C_6)$alkyl-OC(=O)-R^{22}, $-(C_0-C_6)$alkyl-C(=O)-OR^{22}, $-O-(C_1-C_6)$-alkyl-OC(=O)-R^{22}, $-O-(C_1-C_6)$alkyl-C(=O)-OR^{22}, $-(C_0-C_6)$alkyl-C(=O)-R^{22}, $-O-(C_1-C_6)$alkyl-C(=O)-R^{22}, $-(C_0-C_6)$alkyl-NR^{22}-C(=O)-OR^{23}, $-(C_0-C_6)$alkyl-O-C(=O)-

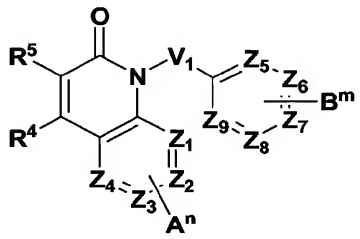
$NR^{22}R^{23}$, $-(C_0-C_6)$alkyl-NR^{22}-C(=NR^{23})-$NR^{24}R^{25}$, $-(C_0-C_6)$alkyl-NR^{22}-C(=O)-$NR^{23}R^{24}$ and $-(C_0-C_6)$alkyl-NR^{22}-C(=S)-$NR^{23}R^{24}$;

m is an integer from 1 to 5;

R^{22}, R^{23}, R^{24} and R^{25} are each independently selected from hydrogen or an optionally substituted radical selected from the group of $-(C_1-C_6)$alkylhalo, $-(C_1-C_6)$alkyl, $-(C_1-C_6)$alkylcyano, $-(C_2-C_6)$alkynyl, $-(C_2-C_6)$alkenyl, $-(C_3-C_7)$cycloalkyl, $-(C_4-C_{10})$-alkylcycloalkyl, heteroaryl, $-(C_1-C_6)$alkylheteroaryl, aryl, $-(C_1-C_6)$alkylaryl, $-(C_2-C_6)$-alkynyl-(C_3-C_7)cycloalkyl, $-(C_2-C_6)$alkynyl-heteroaryl, $-(C_2-C_6)$alkynyl-aryl, $-(C_2-C_6)$-alkenyl-(C_3-C_7)cycloalkyl, $-(C_2-C_6)$alkenyl-heteroaryl or $-(C_2-C_6)$alkenyl-aryl; and

R^{22}, R^{23}, R^{24} and R^{25} may be taken together to form an optionally substituted 3 to 10 membered non-aromatic heterocyclic ring or an optionally substituted 5 to 10 membered aromatic heterocyclic ring.

In a preferred aspect of Formula (III-a), the invention provides a compound according to Formula (III-b),



(III-b)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

V_1 is an optionally substituted radical selected from the group of $-(C_1-C_6)$alkyl-, $-(C_2-C_6)$alkynyl-, $-(C_2-C_6)$alkenyl-, $-(C_3-C_7)$cycloalkyl-, $-(C_3-C_8)$cycloalkenyl-, $-(C_1-C_6)$-alkylhalo-, $-(C_1-C_6)$alkyl-C(=O)-(C_0-C_6)alkyl-, $-(C_1-C_6)$alkyl-C(=O)-(C_2-C_6)alkynyl-, $-(C_1-C_6)$alkyl-C(=O)-(C_2-C_6)alkenyl-, $-(C_1-C_6)$alkyl-C(=O)-(C_3-C_7)cycloalkyl-, $-(C_1-C_6)$alkyl-C(=O)-(C_4-C_{10})alkylcycloalkyl-, $-(C_1-C_6)$alkyl-C(=O)O-(C_0-C_6)alkyl-, $-(C_1-C_6)$alkyl-C(=O)O-(C_2-C_6)alkynyl-, $-(C_1-C_6)$alkyl-C(=O)O-(C_2-C_6)alkenyl-, $-(C_1-C_6)$-alkyl-C(=O)O-(C_3-C_7)cycloalkyl-, $-(C_1-C_6)$alkyl-C(=O)O-(C_4-C_{10})alkylcycloalkyl-,

-(C_1-C_6)alkyl-C(=O)NR^7-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-C(=O)NR^7-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-O-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-O-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-O-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-O-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-O-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)-alkyl-S-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-S-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-S-(C_2-C_6)-alkenyl-, -(C_1-C_6)alkyl-S-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-S-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-S(O)-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-S(O)-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-S(O)-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-S(O)-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-S(O)-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-$S(O)_2$-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-$S(O)_2$-(C_2-C_6)-alkynyl-, -(C_1-C_6)alkyl-$S(O)_2$-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-$S(O)_2$-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-$S(O)_2$-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-$S(O)_2N^7$-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-$S(O)_2N^7$-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-$S(O)_2N^7$-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-$S(O)_2N^7$-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-$S(O)_2N^7$-(C_4-C_{10})alkyl-cycloalkyl-, -(C_1-C_6)alkyl-NR^7-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-NR^7-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-NR^7-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-NR^7-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=O)-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7C(=O)-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-NR^7C(=O)-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-NR^7C(=O)-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=O)-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=O)NR^8-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7C(=O)NR^8-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-NR^7C(=O)NR^8-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-NR^7C(=O)-NR^8-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=O)NR^8-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-$NR^7S(O)_2$-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-$NR^7S(O)_2$-(C_2-C_6)alkynyl-, -(C_1-C_6)-alkyl-$NR^7S(O)_2$-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-$NR^7S(O)_2$-(C_3-C_7)cycloalkyl-, -(C_1-C_6)-alkyl-$NR^7S(O)_2$-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=S)NR^8-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7C(=S)NR^8-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-NR^7C(=S)NR^8-(C_2-C_6)-alkenyl-, -(C_1-C_6)alkyl-NR^7C(=S)NR^8-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=S)-NR^8-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-OC(=O)-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-OC(=O)-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-OC(=O)-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-OC(=O)-(C_3-C_7)cycloalkyl-, -(C_1-C_6)alkyl-OC(=O)-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)-alkyl-OC(=O)NR^7-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-OC(=O)NR^7-(C_2-C_6)alkynyl-, -(C_1-C_6)-alkyl-OC(=O)NR^7-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-OC(=O)NR^7-(C_3-C_7)cycloalkyl-,

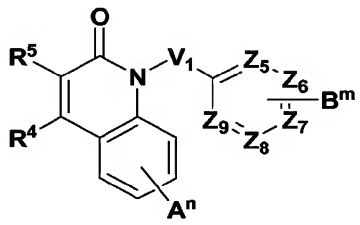
-(C_1-C_6)alkyl-OC(=O)NR^7-(C_4-C_{10})alkylcycloalkyl-, -(C_1-C_6)alkyl-NR^7C(=O)O-(C_0-C_6)alkyl-, -(C_1-C_6)alkyl-NR^7C(=O)O-(C_2-C_6)alkynyl-, -(C_1-C_6)alkyl-NR^7C(=O)O-(C_2-C_6)alkenyl-, -(C_1-C_6)alkyl-NR^7C(=O)O-(C_3-C_7)cycloalkyl- and -(C_1-C_6)alkyl-NR^7C(=O)O-(C_4-C_{10})alkylcycloalkyl- ;

R^2 is selected from the group of hydrogen, halogen, -CN, -CF_3, and an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_2-C_6)alkenyl, -(C_2-C_6)-alkynyl, -(C_1-C_6)alkylhalo, -(C_3-C_7)cycloalkyl, -(C_1-C_6)alkylcyano, -O-(C_1-C_6)alkyl, -O-(C_1-C_6)alkylhalo, -O-(C_1-C_6)alkylcyano, -O-(C_3-C_6)alkynyl, -O-(C_3-C_7)cycloalkyl, -O-(C_2-C_6)alkyl-OR^{26}, -O-(C_1-C_6)alkyl-heteroaryl, -O-(C_0-C_6)alkylaryl, -(C_0-C_6)alkyl-OR^{26}, -O-heteroaryl, -heteroaryl, -(C_1-C_6)alkyl-heteroaryl, -aryl, -O-aryl, -(C_1-C_6)-alkylaryl, -(C_1-C_6)alkylhalo-OR^{26}, -(C_0-C_6)alkyl-SR^{26}, -(C_0-C_6)alkyl-S(=O)$_2$-R^{26}, -(C_0-C_6)alkyl-$NR^{26}R^{27}$, -O-(C_2-C_6)alkyl-$NR^{26}R^{27}$, -(C_0-C_6)alkyl-S(=O)$_2$$NR^{26}R^{27}$, -($C_0$-$C_6$)-alkyl-$NR^{26}$-S(=O)$_2$$R^{27}$, -($C_0$-$C_6$)alkyl-C(=O)-$NR^{26}R^{27}$, -($C_0$-$C_6$)alkyl-$NR^{26}$C(=O)-$R^{27}$, -O-($C_1$-$C_6$)alkylC(=O)-$NR^{26}R^{27}$, -O-($C_1$-$C_6$)alkyl-$NR^{26}$C(=O)-$R^{27}$ and -(C_0-C_6)alkyl-C(=O)-R^{26};

R^{26} and R^{27} are each independently hydrogen or an optionally substituted radical selected from the group of -(C_1-C_6)alkylhalo, -(C_1-C_6)alkylcyano, -(C_0-C_6)alkyl, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_4-C_{10})alkylcycloalkyl, heteroaryl, -(C_1-C_6)alkylheteroaryl, aryl, -(C_1-C_6)alkylaryl, -(C_2-C_6)alkynyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkynyl-heteroaryl, -(C_2-C_6)alkynyl-aryl, -(C_2-C_6)alkenyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkenyl-heteroaryl and -(C_2-C_6)alkenyl-aryl; and

R^{26} and R^{27} may be taken together to form an optionally substituted 3 to 10 membered non-aromatic heterocyclic ring or an optionally substituted 5 to 10 membered aromatic heterocyclic ring.

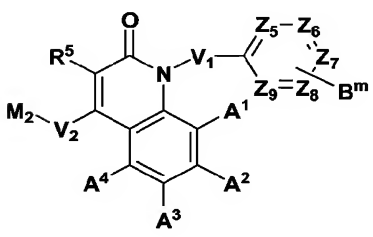
In a further preferred aspect of Formula (III-b), the invention provides a compound of Formula (III-c),



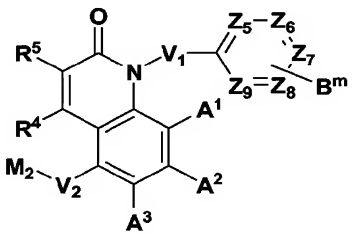
(III-c)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof.

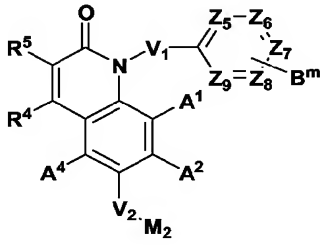
In a further preferred aspect of Formula (III-c), the invention provides a compound according to any one of (III-c1), (III-c2) or (III-c3),



(III-c1)



(III-c2)



(III-c2)

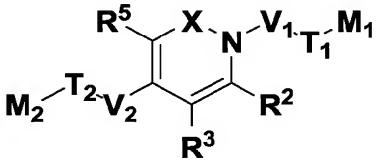
a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

Z_5, Z_6, Z_7, Z_8 and Z_9 are selected from C or N, provided that at least 2 carbons are present and that a free position may further be substituted by 1 to 5 radicals B^m ; and

R^4, R^5, A^1, A^2, A^3 and A^4 are each independently selected from the group of hydrogen, halogen, -CN, -CF_3, -OCF_3, and an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_3-C_8)-cycloalkenyl, -(C_1-C_6)alkylhalo, -(C_0-C_3)alkyl-O-(C_1-C_6)alkyl, -(C_0-C_3)alkyl-O-(C_2-C_6)alkynyl, -(C_0-C_3)alkyl-O-(C_2-C_6)alkenyl, -(C_0-C_3)alkyl-O-(C_3-C_7)cycloalkyl, -(C_0-C_3)alkyl-O-(C_4-C_{10})alkylcycloalkyl, -(C_0-C_3)alkyl-O-(C_1-C_6)alkylhalo, -S-(C_1-C_6)alkyl,

-S-(C_2-C_6)alkynyl, -S-(C_2-C_6)alkenyl, -S-(C_3-C_7)cycloalkyl, -S-(C_4-C_{10})-alkylcycloalkyl, -(C_0-C_3)alkyl-$NR^{18}R^{19}$, -(C_0-C_3)alkyl-$S(O)_2NR^{18}R^{19}$, -(C_0-C_3)alkyl-$NR^{18}S(O)_2R^{19}$, -(C_0-C_3)alkyl-$C(=O)R^{18}$, -(C_0-C_3)alkyl-$C(=O)OR^{18}$, -(C_0-C_3)alkyl-$C(=O)NR^{18}R^{19}$, -(C_0-C_3)alkyl-$NR^{18}C(=O)R^{19}$, -O-(C_0-C_3)alkyl-$S(O)_2NR^{18}R^{19}$, -O-(C_0-C_3)alkyl-$NR^{18}S(O)_2R^{19}$, -O-(C_0-C_3)alkyl-$C(=O)R^{18}$, -O-(C_0-C_3)alkyl-$C(=O)OR^{18}$, -O-(C_0-C_3)alkyl-$C(=O)NR^{18}R^{19}$ and -O-(C_0-C_3)alkyl-$NR^{18}C(=O)R^{19}$.

In a third preferred aspect of Formula (I), the invention provides a compound according to Formula (IV)



(IV)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

X is selected from C(=O) and $S(O)_2$;

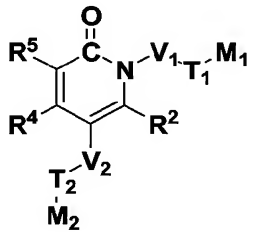
R^2, R^3 and R^5 are each independently selected from the group of hydrogen, halogen, -CN, -OH, $-NO_2$, $-CF_3$, -SH, $-NH_2$, and an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_1-C_6)alkylhalo, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_1-C_6)alkylcyano, -O-(C_1-C_6)alkyl, -O-(C_1-C_6)alkylhalo, -O-(C_1-C_6)-alkylcyano, -O-(C_3-C_6)alkynyl, -O-(C_3-C_7)cycloalkyl, -O-(C_2-C_6)alkenyl, -O-(C_2-C_6)-alkyl-OR^{18}, -O-(C_1-C_6)alkyl-heteroaryl, -O-(C_0-C_6)alkylaryl, -(C_0-C_6)alkyl-OR^{18}, -(C_3-C_7)cycloalkyl-(C_1-C_6)alkyl, -O-(C_3-C_7)cycloalkyl-(C_1-C_6)alkyl, -O-heteroaryl, heteroaryl, -(C_1-C_6)alkyl-heteroaryl, aryl, -O-aryl, -(C_1-C_6)alkylaryl, -(C_1-C_6)alkylhalo-OR^{18}, -(C_3-C_6)alkynyl-OR^{18}, -(C_3-C_6)alkenyl-OR^{18}, -(C_0-C_6)alkyl-SR^{18}, -O-(C_2-C_6)-alkyl-SR^{18}, -(C_1-C_6)alkyl-$S(=O)R^{18}$, -O-(C_1-C_6)alkyl-$S(=O)R^{18}$, -(C_0-C_6)alkyl-$S(=O)_2R^{18}$, -O-(C_1-C_6)alkyl-$S(=O)_2R^{18}$, -(C_0-C_6)alkyl-$NR^{18}R^{19}$, -(C_0-C_3)alkyl-O-(C_2-C_6)alkyl-$NR^{18}R^{19}$, -(C_0-C_6)alkyl-$S(=O)_2NR^{18}R^{19}$, -(C_0-C_6)alkyl-NR^{18}-$S(=O)_2R^{19}$, -(C_0-C_3)alkyl-O-(C_1-C_6)alkyl-$S(=O)_2NR^{18}R^{19}$, -(C_0-C_3)alkyl-O-(C_1-C_6)alkyl-NR^{18}-$S(=O)_2R^{19}$, -(C_0-C_6)alkyl-C(=O)-$NR^{18}R^{19}$, -(C_0-C_6)alkyl-$NR^{18}C(=O)$-R^{19}, -(C_0-C_3)-

alkyl-O-(C_1-C_6)alkylC(=O)-$NR^{18}R^{19}$, -(C_0-C_3)alkyl-O-(C_1-C_6)alkyl-NR^{18}C(=O)-R^{19}, -(C_0-C_6)alkyl-OC(=O)-R^{18}, -(C_0-C_6)alkyl-C(=O)-OR^{18}, -O-(C_1-C_6)alkyl-OC(=O)-R^{18}, -O-(C_1-C_6)alkyl-C(=O)-OR^{18}, -(C_0-C_6)alkyl-C(=O)-R^{18}, -O-(C_1-C_6)alkyl-C(=O)-R^{18}, -(C_0-C_6)alkyl-NR^{18}-C(=O)-OR^{19}, -(C_0-C_6)alkyl-O-C(=O)-$NR^{18}R^{19}$, -(C_0-C_6)alkyl-NR^{18}-C(=NR^{19})-$NR^{20}R^{21}$, -(C_0-C_6)alkyl-NR^{18}-C(=O)-$NR^{19}R^{20}$ and -(C_0-C_6)alkyl-NR^{18}-C(=S)-$NR^{19}R^{20}$;

R^{18}, R^{19}, R^{20} and R^{21} are each independently selected from hydrogen and an optionally substituted radical selected from the group of -(C_1-C_6)alkylhalo, -(C_1-C_6)alkyl, -(C_1-C_6)alkylcyano, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_4-C_{10})-alkylcycloalkyl, heteroaryl, -(C_1-C_6)alkylheteroaryl, aryl, -(C_1-C_6)alkylaryl, -(C_2-C_6)-alkynyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkynyl-heteroaryl, -(C_2-C_6)alkynyl-aryl, -(C_2-C_6)alkenyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkenyl-heteroaryl and -(C_2-C_6)alkenyl-aryl; and

R^{18}, R^{19}, R^{20} and R^{21} may be taken together to form an optionally substituted 3 to 10 membered non-aromatic heterocyclic ring or an optionally substituted 5 to 10 membered aromatic heterocyclic ring.

In a fourth preferred aspect of Formula (I), the invention provides a compound of Formula (V)



(V)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

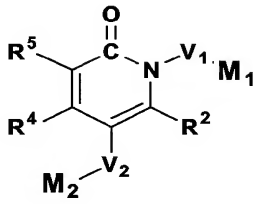
R^2, R^4 and R^5 are each independently selected from the group of hydrogen, halogen, -CN, -OH, -NO_2, -CF_3, -SH, -NH_2, and an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_1-C_6)alkylhalo, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_1-C_6)alkylcyano, -O-(C_1-C_6)alkyl, -O-(C_1-C_6)alkylhalo, -O-(C_1-C_6)-alkylcyano, -O-(C_3-C_6)alkynyl, -O-(C_3-C_7)cycloalkyl, -O-(C_2-C_6)alkenyl, -O-(C_2-

C_6)alkyl-OR^{18}, -O-(C_1-C_6)alkyl-heteroaryl, -O-(C_0-C_6)alkylaryl, -(C_0-C_6)alkyl-OR^{18}, -(C_3-C_7)cycloalkyl-(C_1-C_6)alkyl, -O-(C_3-C_7)cycloalkyl-(C_1-C_6)alkyl, -O-heteroaryl, heteroaryl, -(C_1-C_6)alkyl-heteroaryl, aryl, -O-aryl, -(C_1-C_6)alkylaryl, -(C_1-C_6)alkylhalo-OR^{18}, -(C_3-C_6)alkynyl-OR^{18}, -(C_3-C_6)alkenyl-OR^{18}, -(C_0-C_6)alkyl-SR^{18}, -O-(C_2-C_6)-alkyl-SR^{18}, -(C_1-C_6)alkyl-S(=O)R^{18}, -O-(C_1-C_6)alkyl-S(=O)R^{18}, -(C_0-C_6)alkyl-S(=O)$_2R^{18}$, -O-(C_1-C_6)alkyl-S(=O)$_2R^{18}$, -(C_0-C_6)alkyl-$NR^{18}R^{19}$, -(C_0-C_3)alkyl-O-(C_2-C_6)alkyl-$NR^{18}R^{19}$, -(C_0-C_6)alkyl-S(=O)$_2NR^{18}R^{19}$, -(C_0-C_6)alkyl-NR^{18}-S(=O)$_2R^{19}$, -(C_0-C_3)alkyl-O-(C_1-C_6)alkyl-S(=O)$_2NR^{18}R^{19}$, -(C_0-C_3)alkyl-O-(C_1-C_6)alkyl-NR^{18}-S(=O)$_2R^{19}$, -(C_0-C_6)alkyl-C(=O)-$NR^{18}R^{19}$, -(C_0-C_6)alkyl-NR^{18}C(=O)-R^{19}, -(C_0-C_3)alkyl-O-(C_1-C_6)alkylC(=O)-$NR^{18}R^{19}$, -(C_0-C_3)alkyl-O-(C_1-C_6)alkyl-NR^{18}C(=O)-R^{19}, -(C_0-C_6)alkyl-OC(=O)-R^{18}, -(C_0-C_6)alkyl-C(=O)-OR^{18}, -O-(C_1-C_6)alkyl-OC(=O)-R^{18}, -O-(C_1-C_6)alkyl-C(=O)-OR^{18}, -(C_0-C_6)alkyl-C(=O)-R^{18}, -O-(C_1-C_6)alkyl-C(=O)-R^{18}, -(C_0-C_6)alkyl-NR^{18}-C(=O)-OR^{19}, -(C_0-C_6)alkyl-O-C(=O)-$NR^{18}R^{19}$, -(C_0-C_6)alkyl-NR^{18}-C(=NR^{19})-$NR^{20}R^{21}$, -(C_0-C_6)alkyl-NR^{18}-C(=O)-$NR^{19}R^{20}$ and -(C_0-C_6)alkyl-NR^{18}-C(=S)-$NR^{19}R^{20}$;

R^{18}, R^{19}, R^{20} and R^{21} are each independently selected from hydrogen and an optionally substituted radical selected from the group of -(C_1-C_6)alkylhalo, -(C_1-C_6)alkyl, -(C_1-C_6)alkylcyano, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_4-C_{10})-alkylcycloalkyl, heteroaryl, -(C_1-C_6)alkylheteroaryl, aryl, -(C_1-C_6)alkylaryl, -(C_2-C_6)-alkynyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkynyl-heteroaryl, -(C_2-C_6)alkynyl-aryl, -(C_2-C_6)-alkenyl-(C_3-C_7)cycloalkyl, -(C_2-C_6)alkenyl-heteroaryl and -(C_2-C_6)alkenyl-aryl; and

R^{18}, R^{19}, R^{20} and R^{21} may be taken together to form an optionally substituted 3 to 10 membered non-aromatic heterocyclic ring or an optionally substituted 5 to 10 membered aromatic heterocyclic ring.

In a further preferred aspect of Formula (V), the invention provides a compound according to Formula (V-a),



(V-a)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

V_1 is not a covalent bond ;

V_2 is selected from the group of a covalent bond, -O-, -C(=O)-, -C(=O)O-, -C(=O)NR^{10}-, -S-, -S(O)-, -$S(O)_2$-, -$S(O)_2NR^{10}$-, -NR^{10}-, -NR^{10}C(=O)-, -NR^{10}C(=O)NR^{11}-, -$NR^{10}S(O)_2$-, -NR^{10}C(=S)NR^{11}-, -OC(=O)-, -OC(=O)NR^{10}, -NR^{10}C(=O)O-, and an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_3-C_8)-cycloalkenyl, -(C_1-C_6)alkylhalo, -O-(C_1-C_6)alkyl, -O-(C_2-C_6)alkynyl, -O-(C_2-C_6)-alkenyl, -O-(C_3-C_7)cycloalkyl, -O-(C_4-C_{10})alkylcycloalkyl, -C(=O)-(C_1-C_6)alkyl, -C(=O)-(C_2-C_6)alkynyl, -C(=O)-(C_2-C_6)alkenyl, -C(=O)-(C_3-C_7)alkylcycloalkyl, -C(=O)-(C_4-C_{10})cycloalkyl, -C(=O)O-(C_1-C_6)alkyl, -C(=O)O-(C_2-C_6)alkynyl, -C(=O)O-(C_2-C_6)alkenyl, -C(=O)O-(C_3-C_7)cycloalkyl, -C(=O)O-(C_4-C_{10})-alkylcycloalkyl, -C(=O)NR^{10}-(C_1-C_6)alkyl, -C(=O)NR^{10}-(C_2-C_6)alkynyl, -C(=O)NR^{10}-(C_2-C_6)alkenyl, -C(=O)NR^{10}-(C_3-C_7)cycloalkyl, -C(=O)NR^{10}-(C_4-C_{10})-alkylcycloalkyl, -S-(C_1-C_6)alkyl, -S-(C_2-C_6)alkynyl, -S-(C_2-C_6)alkenyl, -S-(C_3-C_7)cycloalkyl, -S-(C_4-C_{10})alkylcycloalkyl, -S(O)-(C_1-C_6)alkyl, -O-(C_2-C_6)alkynyl, -S(O)-(C_2-C_6)alkenyl, -S(O)-(C_3-C_7)cycloalkyl, -S(O)-(C_4-C_{10})alkylcycloalkyl, -$S(O)_2$-(C_1-C_6)alkyl, -$S(O)_2$-(C_2-C_6)alkynyl, -$S(O)_2$-(C_2-C_6)alkenyl, -$S(O)_2$-(C_3-C_7)cycloalkyl, -$S(O)_2$-(C_4-C_{10})alkylcycloalkyl, -$S(O)_2NR^{10}$-(C_1-C_6)alkyl, -$S(O)_2NR^{10}$-(C_2-C_6)alkynyl, -$S(O)_2NR^{10}$-(C_2-C_6)alkenyl, -$S(O)_2NR^{10}$-(C_3-C_7)cycloalkyl, -$S(O)_2NR^{10}$-(C_4-C_{10})alkylcycloalkyl, -NR^{10}-(C_1-C_6)alkyl, -NR^{10}-(C_2-C_6)alkynyl, -NR^{10}-(C_2-C_6)alkenyl, -NR^{10}-(C_3-C_7)cycloalkyl, -NR^{10}-(C_4-C_{10})alkylcycloalkyl, -NR^{10}C(=O)-(C_1-C_6)alkyl, -NR^{10}C(=O)-(C_2-C_6)alkynyl, -NR^{10}C(=O)-(C_2-C_6)alkenyl, -NR^{10}C(=O)-

$(C_3\text{-}C_7)$cycloalkyl, $-NR^{10}C(=O)\text{-}(C_4\text{-}C_{10})$alkylcycloalkyl, $-NR^{10}C(=O)NR^{11}\text{-}(C_1\text{-}C_6)$-alkyl, $-NR^{10}C(=O)NR^{11}\text{-}(C_2\text{-}C_6)$alkynyl, $-NR^{10}C(=O)NR^{11}\text{-}(C_2\text{-}C_6)$alkenyl, $-NR^{10}C(=O)NR^{11}\text{-}(C_3\text{-}C_7)$cycloalkyl, $-NR^{10}C(=O)NR^{11}\text{-}(C_4\text{-}C_{10})$alkylcycloalkyl, $-NR^{10}S(O)_2\text{-}(C_1\text{-}C_6)$alkyl, $-NR^{10}S(O)_2\text{-}(C_2\text{-}C_6)$alkynyl, $-NR^{10}S(O)_2\text{-}(C_2\text{-}C_6)$alkenyl, $-NR^{10}S(O)_2\text{-}(C_3\text{-}C_7)$cycloalkyl, $-NR^{10}S(O)_2\text{-}(C_4\text{-}C_{10})$alkylcycloalkyl, $-NR^{10}C(=S)NR^{11}$--$(C_1\text{-}C_6)$alkyl, $-NR^{10}C(=S)NR^{11}\text{-}(C_2\text{-}C_6)$alkynyl, $-NR^{10}C(=S)NR^{11}\text{-}(C_2\text{-}C_6)$alkenyl, $-NR^{10}C(=S)NR^{11}\text{-}(C_3\text{-}C_7)$cycloalkyl, $-NR^{10}C(=S)NR^{11}\text{-}(C_4\text{-}C_{10})$alkylcycloalkyl, $-OC(=O)\text{-}(C_1\text{-}C_6)$alkyl, $-OC(=O)\text{-}(C_2\text{-}C_6)$alkynyl, $-OC(=O)\text{-}(C_2\text{-}C_6)$alkenyl, $-OC(=O)\text{-}(C_4\text{-}C_{10})$alkylcycloalkyl, $-OC(=O)\text{-}(C_3\text{-}C_7)$cycloalkyl, $-OC(=O)NR^{10}\text{-}(C_1\text{-}C_6)$alkyl, $-OC(=O)NR^{10}\text{-}(C_2\text{-}C_6)$alkynyl, $-OC(=O)NR^{10}\text{-}(C_2\text{-}C_6)$alkenyl, $-OC(=O)NR^{10}\text{-}(C_4\text{-}C_{10})$-alkylcycloalkyl, $-OC(=O)NR^{10}\text{-}(C_3\text{-}C_7)$cycloalkyl, $-NR^{10}C(=O)O\text{-}(C_1\text{-}C_6)$alkyl, $-NR^{10}C(=O)O\text{-}(C_2\text{-}C_6)$alkynyl, $-NR^{10}C(=O)O\text{-}(C_2\text{-}C_6)$alkenyl, $-NR^{10}C(=O)O\text{-}(C_3\text{-}C_7)$-cycloalkyl, $-NR^{10}C(=O)O\text{-}(C_4\text{-}C_{10})$alkylcycloalkyl, $-NR^{10}C(=NR^{11})NR^{12}\text{-}(C_1\text{-}C_6)$alkyl, $-NR^{10}C(=NR^{11})NR^{12}\text{-}(C_2\text{-}C_6)$alkynyl, $-NR^{10}C(=NR^{11})NR^{12}\text{-}(C_2\text{-}C_6)$alkenyl, $-NR^{10}C(=NR^{11})NR^{12}\text{-}(C_3\text{-}C_7)$cycloalkyl, $-NR^{10}C(=NR^{11})NR^{12}\text{-}(C_4\text{-}C_{10})$alkylcycloalkyl, $-NR^{10}C(=NR^{11})\text{-}(C_1\text{-}C_6)$alkyl, $-NR^{10}C(=NR^{11})\text{-}(C_2\text{-}C_6)$alkynyl, $-NR^{10}C(=NR^{11})\text{-}(C_2\text{-}C_6)$alkenyl, $-NR^{10}C(=NR^{11})\text{-}(C_3\text{-}C_7)$cycloalkyl, $-NR^{10}C(=NR^{11})\text{-}(C_4\text{-}C_{10})$alkylcycloalkyl, $-C(=NR^{10})NR^{11}\text{-}(C_1\text{-}C_6)$alkyl, $-C(=NR^{10})NR^{11}\text{-}(C_2\text{-}C_6)$alkynyl, $-C(=NR^{10})NR^{11}\text{-}(C_2\text{-}C_6)$alkenyl, $-C(=NR^{10})NR^{11}\text{-}(C_3\text{-}C_7)$cycloalkyl and $-C(=NR^{10})NR^{11}\text{-}(C_4\text{-}C_{10})$alkylcycloalkyl; and

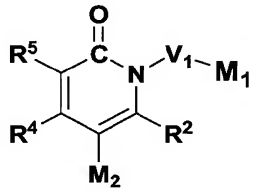
R^2, R^4 and R^5 are each independently selected from the group of hydrogen, halogen, -CN, -OH, $-NO_2$, $-CF_3$, -SH, $-NH_2$, and an optionally substituted radical selected from the group of $-(C_1\text{-}C_6)$alkyl, $-(C_1\text{-}C_6)$alkylhalo, $-(C_2\text{-}C_6)$alkynyl, $-(C_2\text{-}C_6)$alkenyl, $-(C_3\text{-}C_7)$cycloalkyl, $-(C_1\text{-}C_6)$alkylcyano, $-O\text{-}(C_1\text{-}C_6)$alkyl, $-O\text{-}(C_1\text{-}C_6)$alkylhalo, $-O\text{-}(C_1\text{-}C_6)$-alkylcyano, $-O\text{-}(C_3\text{-}C_6)$alkynyl, $-O\text{-}(C_3\text{-}C_7)$cycloalkyl, $-O\text{-}(C_2\text{-}C_6)$alkenyl, $-O\text{-}(C_2\text{-}C_6)$-alkyl-$OR^{18}$, $-O\text{-}(C_1\text{-}C_6)$alkyl-heteroaryl, $-O\text{-}(C_0\text{-}C_6)$alkylaryl, $-(C_0\text{-}C_6)$alkyl-OR^{18}, $-(C_3\text{-}C_7)$cycloalkyl-$(C_1\text{-}C_6)$alkyl, $-O\text{-}(C_3\text{-}C_7)$cycloalkyl-$(C_1\text{-}C_6)$alkyl, -O-heteroaryl, $-(C_1\text{-}C_6)$alkyl-heteroaryl, -O-aryl, $-(C_1\text{-}C_6)$alkylaryl, $-(C_1\text{-}C_6)$alkylhalo-OR^{18}, $-(C_3\text{-}C_6)$-alkynyl-OR^{18}, $-(C_3\text{-}C_6)$alkenyl-OR^{18}, $-(C_0\text{-}C_6)$alkyl-SR^{18}, $-O\text{-}(C_2\text{-}C_6)$alkyl-$SR^{18}$, $-(C_1\text{-}C_6)$alkyl-$S(=O)R^{18}$, $-O\text{-}(C_1\text{-}C_6)$alkyl-$S(=O)R^{18}$, $-(C_0\text{-}C_6)$alkyl-$S(=O)_2R^{18}$, $-O\text{-}(C_1\text{-}C_6)$-alkyl-$S(=O)_2R^{18}$, $-(C_0\text{-}C_6)$alkyl-$NR^{18}R^{19}$, $-(C_0\text{-}C_3)$alkyl-O-$(C_2\text{-}C_6)$alkyl-$NR^{18}R^{19}$, $-(C_0\text{-}C_6)$alkyl-$S(=O)_2NR^{18}R^{19}$, $-(C_0\text{-}C_6)$alkyl-$NR^{18}\text{-}S(=O)_2R^{19}$, $-(C_0\text{-}C_3)$alkyl-O-$(C_1\text{-}C_6)$alkyl-

$S(=O)_2NR^{18}R^{19}$, $-(C_0\text{-}C_3)$alkyl-O-$(C_1\text{-}C_6)$alkyl-NR^{18}-$S(=O)_2R^{19}$, $-(C_0\text{-}C_6)$alkyl-$C(=O)$-$NR^{18}R^{19}$, $-(C_0\text{-}C_6)$alkyl-$NR^{18}C(=O)$-R^{19}, $-(C_0\text{-}C_3)$alkyl-O-$(C_1\text{-}C_6)$alkyl$C(=O)$-$NR^{18}R^{19}$, $-(C_0\text{-}C_3)$alkyl-O-$(C_1\text{-}C_6)$alkyl-$NR^{18}C(=O)$-R^{19}, $-(C_0\text{-}C_6)$alkyl-$OC(=O)$-R^{18}, $-(C_0\text{-}C_6)$-alkyl-$C(=O)$-OR^{18}, -O-$(C_1\text{-}C_6)$alkyl-$OC(=O)$-R^{18}, -O-$(C_1\text{-}C_6)$alkyl-$C(=O)$-OR^{18}, $-(C_0\text{-}C_6)$alkyl-$C(=O)$-R^{18} and -O-$(C_1\text{-}C_6)$alkyl-$C(=O)$-R^{18}.

In a further preferred aspect of Formula (V-a), the invention provides a compound according to Formula (V-a), wherein :

V_2 is selected from the group of a covalent bond, -O-, $-C(=O)$-, $-C(=O)O$-, $-C(=O)NR^{10}$-, -S-, -S(O)-, $-S(O)_2$-, $-S(O)_2NR^{10}$-, $-NR^{10}$-, $-NR^{10}C(=O)$-, $-NR^{10}C(=O)NR^{11}$-, $-NR^{10}S(O)_2$-, $-NR^{10}C(=S)NR^{11}$-, and an optionally substituted radical selected from the group of $-(C_1\text{-}C_6)$alkyl, $-(C_2\text{-}C_6)$alkynyl, $-(C_2\text{-}C_6)$alkenyl, $-(C_3\text{-}C_7)$cycloalkyl, $-(C_3\text{-}C_8)$cycloalkenyl, $-(C_1\text{-}C_6)$alkylhalo, -O-$(C_1\text{-}C_6)$alkyl, -O-$(C_3\text{-}C_7)$cycloalkyl, $-C(=O)$-$(C_1\text{-}C_6)$alkyl, $-C(=O)$-$(C_4\text{-}C_{10})$cycloalkyl, $-C(=O)O$-$(C_1\text{-}C_6)$-alkyl, $-C(=O)O$-$(C_3\text{-}C_7)$cycloalkyl, $-C(=O)NR^{10}$-$(C_1\text{-}C_6)$alkyl, $-C(=O)NR^{10}$-$(C_3\text{-}C_7)$-cycloalkyl, -S-$(C_1\text{-}C_6)$alkyl, -S-$(C_3\text{-}C_7)$cycloalkyl, -S(O)-$(C_1\text{-}C_6)$alkyl, -S(O)-$(C_3\text{-}C_7)$-cycloalkyl, $-S(O)_2$-$(C_1\text{-}C_6)$alkyl, $-S(O)_2$-$(C_3\text{-}C_7)$cycloalkyl, $-S(O)_2NR^{10}$-$(C_1\text{-}C_6)$alkyl, $-S(O)_2NR^{10}$-$(C_3\text{-}C_7)$cycloalkyl, $-NR^{10}$-$(C_1\text{-}C_6)$alkyl, $-(C_3\text{-}C_7)$cycloalkyl, $-NR^{10}C(=O)$-$(C_1\text{-}C_6)$alkyl, $-NR^{10}C(=O)$-$(C_3\text{-}C_7)$cycloalkyl, $-NR^{10}C(=O)NR^{11}$-$(C_1\text{-}C_6)$alkyl, $-NR^{10}C(=O)NR^{11}$-$(C_3\text{-}C_7)$cycloalkyl, $-NR^{10}S(O)_2$-$(C_1\text{-}C_6)$alkyl and $-NR^{10}S(O)_2$-$(C_3\text{-}C_7)$cycloalkyl.

In a further preferred aspect of Formula (V-a), the invention provides a compound of Formula (V-b)



(V-b)

a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

V_1 is an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl, -(C_1-C_6)alkylhalo, -(C_1-C_6)alkyl-C(=O)-(C_0-C_6)alkyl, -(C_1-C_6)alkyl-C(=O)NR^7-(C_0-C_6)alkyl, -(C_1-C_6)alkyl-O-(C_0-C_6)-alkyl, -(C_0-C_6)alkyl-$S(O)_2$-(C_0-C_6)alkyl, -(C_1-C_6)alkyl-$S(O)_2NR^7$-(C_0-C_6)alkyl, -(C_1-C_6)alkyl-NR^7-(C_0-C_6)alkyl, -(C_1-C_6)alkyl-NR^7C(=O)-(C_0-C_6)alkyl and -(C_1-C_6)alkyl-$NR^7S(O)_2$-(C_0-C_6)alkyl;

R^7 is a radical selected from the group of hydrogen, -(C_1-C_6)alkyl, -(C_1-C_6)alkylhalo, -(C_2-C_6)alkynyl, -(C_2-C_6)alkenyl, -(C_3-C_7)cycloalkyl or -(C_1-C_6)alkylcyano; and

M_1 and M_2 are each independently hydrogen or an optionally substituted radical selected from the group of aryl, heteroaryl and (C_3-C_7)cycloalkyl.

In a further preferred aspect of Formula (V-b), the invention provides a compound according to Formula (V-b) wherein :

V_1 is -(C_1-C_6)alkyl, optionally substituted by one or more -OCH_3, -OCF_3, -CF_3, fluoro or cyano radicals ; and

M_1 and M_2 are each independently an optionally substituted radical selected from hydrogen, aryl, thienyl, pyridyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, benzoimidazolyl, benzooxazolyl, benzothiazolyl, thionaphtyl, indolyl, pyrimidinyl, quinolyl, cyclohexyl and cyclopentyl.

Most preferably, the invention relates to compounds according to Formulla (I), a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof, wherein :

X is C(=O);

Y is selected from -C(R^4)=C(R^5)-, -C(R^5)=N- and -N=C(R^5)- ;

R^1 is an optionally substituted radical selected from the group of -(C_1-C_6)alkyl, -(C_1-C_6)alkylhalo and a radical -V_1-T_1-M_1;

T_1, V_1 are each independently a covalent bond or an optionally substituted radical, preferably substituted with hydroxy, halo and halo(C_1-C_6)alkyl, selected from the group of -(C_1-C_6)alkyl- ; -(C_2-C_6)alkenyl-, -(C_2-C_6)alkynyl- ; -(C_1-C_6)alkyl-C(=O)-(C_0-

C_6)alkyl- ; -(C_1-C_6)alkyl-C(=O)NR^7-(C_0-C_6)alkyl- wherein R^7 is hydrogen or -(C_1-C_6)-alkyl- ; and -(C_1-C_6)alkyl-O-(C_0-C_6)alkyl- ;

R^2, R^3, R^4 and R^5 are each independently selected from the group of hydrogen, halogen, -CN, -NO_2, -C(=O)OR^{10}, -OR^{10}, and an optionally substituted radical, preferably substituted with hydroxy, selected from the group of -(C_1-C_6)alkyl and a radical -V_2-T_2-M_2 ;

T_2, V_2 are each independently a covalent bond or a radical selected from the group of -O- ; -C(=O)- ; -NR^{10}- and an optionally substituted radical, preferably substituted with hydroxy, selected from the group of -(C_1-C_6)alkyl- ; -(C_2-C_6)alkenyl- ; -(C_2-C_6)alkynyl-; -(C_0-C_6)alkyl-O-(C_1-C_6)alkyl- ; and -(C_0-C_6)alkyl-NR^{10}-(C_1-C_6)alkyl- wherein R^{10} is preferably hydrogen or (C_1-C_6)alkyl;

(R^2 and R^3) or (R^4 and R^5) taken together may form an aryl optionally substituted with n radicals A^n equal to -V_2-M_2 ;

M_1 and M_2 are each independently selected from the group of hydrogen, an optionally substituted -(C_1-C_6)alkyl-radical and an optionally substituted 3 to 10 membered ring selected from the group of (C_{1-6})cycloalkyl ; aryl, preferably phenyl or naphthyl ; heteroaryl and heterocyclic, preferably pyridinyl, indolyl, , imidazolyl, oxadiazolyl, isoxazolyl, furyl, thienyl, thiazolyl, benzothiazolyl, pyridinyl, pyrimidinyl, indolyl, quinolinyl, quinoxalinyl, benzoxazolyl, benzodioxolyl, benzotetrahydrofuryl and benzothienyl ; wherein the optional substitution on any of the aforementioned rings is selected from the group of (C_1-C_6)alkyl; (C_1-C_6)alkyloxy; hydroxy(C_1-C_6)alkyloxy;(C_1-C_6)alkyloxy(C_1-C_6)alkyl; (C_1-C_6)alkyloxy(C_1-C_6)alkyloxy; (C_1-C_6)alkyloxycarbonyl; (C_1-C_6)alkyloxycarbonyl(C_1-C_6)alkyl; (C_1-C_6)alkyloxycarbonyloxy; (C_1-C_6)alkyloxycarbonyl(C_1-C_6)alkyloxy; (C_1-C_6)alkylcarbonyl; (C_1-C_6)alkylcarbonyl(C_1-C_6)alkyloxy; (C_1-C_6)alkylcarbonyloxy; (C_1-C_6)alkylthieno;

(C_1-C_6)alkylsulfonyl ; heterocyclic-sulfonyl, preferably morpholinylsulfonyl and pyrrolidinylsulfonyl; (C_1-C_6)alkylsulfonylamino; (C_1-C_6)alkenyl; aryl, preferably phenyl; carboxyl(C_1-C_6)alkyl; carbonyl(C_1-C_6)alkyloxy; halo, preferably fluoro and chloro; hydroxy; hydroxy(C_1-C_6)alkyl; phenyl(C_1-C_6)alkyloxy; cyano;cyano(C_1-C_6)alkyloxy; trifluoro(C_1-C_6)alkyl; trifluoro(C_1-C_6)alkyloxy; amino; amino(C_1-C_6)alkyloxy; mono- and di((C_1-C_6)alkyl)amino; mono- and di((C_1-

C_6)alkylcarbonyl)amino; mono- and di((C_1-C_6)alkyloxycarbonyl)amino; mono- and di((C_1-C_6)alkylcarbonyl)amino(C_1-C_6)alkyl; mono- and di((C_1-C_6)alkylsulfonyl)amino(C_1-C_6)alkyloxy; mono- and di((C_1-C_6)alkyl)amino(C_1-C_6)alkyloxy; mono- and di((C_1-C_6)alkylcarbonyl)amino(C_1-C_6)alkyloxy; mono- and di((C_1-C_6)alkyl)aminocarbonyl; mono- and di((C_1-C_6)alkyl)aminocarbonyl(C_1-C_6)alkyl; mono- and di((C_1-C_6)alkyl)aminocarbonyl(C_1-C_6)alkyloxo; mono- and di((C_1-C_6)alkyl)amino(C_1-C_6)alkylamino; nitro; tri(C_1-C_6)alkylsilyl; heterocyclic, preferably morpholinyl; heterocyclic-(C_1-C_6)alkyl, preferably (C_1-C_6)alkyltetrazolyl; and heterocyclic-(C_1-C_6)alkyloxy, the heterocyclic preferably being pyridinyl, morpholinyl, pyrrolidinyl, optionally substituted with oxo, isoxazolyl, imidazolyl, tetrazolyl or thiazolyl ;

R^7, R^8, R^9, R^{10}, R^{11}, R^{12}, R^{13}, R^{14}, R^{15}, R^{16}, R^{17} are each independently hydrogen or an optionally substituted -(C_1-C_6)alkyl-radical ;

A^n is hydrogen or halo ; and

n is an integer equal to 0 or 1.

Particular preferred compounds of the invention are compounds as mentioned in the following list (List of Particular Preferred Compounds), as well as a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof.

1-(4-methoxybenzyl)-2-oxo-4-phenyl-1,2-dihydropyridine-3-carbonitrile
1-(4-methylbenzyl)-2-oxo-4-phenyl-1,2-dihydropyridine-3-carbonitrile
1-(2-methylbenzyl)-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridine-3-carbonitrile
1-cinnamyl-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridine-3-carbonitrile
1-(2,4-difluorobenzyl)-5-(benzofuran-2-yl)pyridin-2(1H)-one
1-benzyl-5-(4-fluorophenyl)pyridin-2(1H)-one
1-(2,4-difluorobenzyl)-5-(4-fluorophenyl)pyridin-2(1H)-one
1-(3-chlorobenzyl)-5-(4-fluorophenyl)pyridin-2(1H)-one
1-benzyl-5-(4-methoxyphenyl)pyridin-2(1H)-one
1-(3-(trifluoromethyl)benzyl)-5-phenylpyridin-2(1H)-one
1-(4-methylbenzyl)-5-phenylpyridin-2(1H)-one
1-(2,4-difluorobenzyl)-5-(thiophen-2-yl)pyridin-2(1H)-one
1-benzyl-5-(4-chlorophenyl)pyridin-2(1H)-one

1-(3-(trifluoromethyl)benzyl)-5-(4-chlorophenyl)pyridin-2(1H)-one
1-(2,4-difluorobenzyl)-5-(4-chlorophenyl)pyridin-2(1H)-one
1-(2,4-dichlorobenzyl)-5-(4-methoxyphenyl)pyrimidin-2(1H)-one
1-(3-chlorobenzyl)-5-phenylpyridin-2(1H)-one
1-(3-chlorobenzyl)-5-(4-methoxyphenyl)pyridin-2(1H)-one
1-Benzyl-5-phenylpyridin-2(*1H)*-one
1-(2,4-difluorobenzyl)-5-phenylpyridin-2(1H)-one
1-Benzyl-5-(3-methoxyphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(3-chlorophenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-cyanophenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(3-nitrophenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(2-fluorophenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(3,4-dimethoxyphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(naphthalen-2-yl)pyridin-2(*1H*)-one
1-Benzyl-5-(2-methoxyphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-m-tolylpyridin-2(*1H*)-one
1-Benzyl-5-(3-chloro-4-isopropoxyphenyl)pyridin-2(*1H*)-one
Ethyl-4-(1-benzyl-6-oxo-1,6-dihydropyridin-3-yl)benzoate
1-Benzyl-5-(2-fluoro-5-methoxyphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-tolyl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-(trifluoromethoxy)phenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-acetylphenyl)pyridin-2(*1H*)-one
2-(4-Fluorobenzyl)isoquinolin-1(*2H*)-one
1-(2-Fluorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Fluorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Nitrobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(3,4-Dichlorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(3-Nitrobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(3-Methoxybenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(Benzo[d]thiazol-2-ylmethyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-isobutoxyphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(2-phenylethynyl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-hydroxyphenyl)pyridin-2(*1H*)-one
1-(4-Methoxybenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
3-((5-(4-Methoxyphenyl)-2-oxopyridin-1(2H)-yl)methyl)benzonitrile
1-(3-Fluorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-(1-phenylethyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-(pyridin-3-ylmethyl)pyridin-2(*1H*)-one

1-Benzyl-5-(4-ethylphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(2,3-dihydro-1-benzofuran-5-yl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-(dimethylamino)phenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(3,4-dimethylphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(3,4-dichlorophenyl)pyridin-2(*1H*)-one
1-((3-(4-Fluorophenyl)-1,2,4-oxadiazol-5-yl)methyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-tert-butylphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(indol-5-yl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-propoxyphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-(trimethylsilyl)phenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(3,5-difluorophenyl)pyridin-2(*1H*)-one
N-(4-Fluorobenzyl)-2-(5-(4-methoxyphenyl)-2-oxopyridin-1(2H)-yl)-N-methylacetamide
1-((5-Fluorobenzo[d]oxazol-2-yl)methyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-methoxyphenyl)-3-methylpyridin-2(*1H*)-one
1-Benzyl-5-(4-methoxyphenyl)-4-methylpyridin-2(*1H*)-one
1-Benzyl-5-(6-methoxypyridin-3-yl)pyridin-2(*1H*)-one
1-Benzyl-5-(4-methoxyphenyl)-3-nitropyridin-2(*1H*)-one
1-(4-Methylbenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(3,4-Difluorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-(Trifluoromethyl)benzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(3-Fluoro-4-methylbenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
Methyl 4-((5-(4-methoxyphenyl)-2-oxopyridin-1(2H)-yl)methyl)benzoate
4-((5-(4-Methoxyphenyl)-2-oxopyridin-1(2H)-yl)methyl)benzonitrile
5-(4-Methoxyphenyl)-1-(naphthalen-2-ylmethyl)pyridin-2(*1H*)-one
1-(3-Fluoro-4-(trifluoromethyl)benzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(3-Chloro-4-fluorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chloro-3-(trifluoromethyl)benzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(2-Fluoro-4-(trifluoromethyl)benzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(2-Fluoro-4-chlorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)quinolin-2(*1H*)-one
1-Benzyl-5-phenethylpyridin-2(*1H*)-one
1-(3-Fluorobenzyl)-3-chloro-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-((5-methylisoxazol-3-yl)methyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(2,5-difluorophenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(3-fluoro-4-methylphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(2-ethoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(quinolin-3-yl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-tolyl)pyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(2-fluorophenyl)pyridin-2(*1H*)-one
Methyl-3-(4-(1-(4-chlorobenzyl)-1,6-dihydro-6-oxopyridin-3-yl)phenyl) propanoate
1-(4-Chlorobenzyl)-5-(4-isobutylphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-sec-butylphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-vinylphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(3-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(2,3-dihydrobenzofuran-5-yl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-acetylphenyl)pyridin-2(*1H*)-one
3-(4-(1-(4-Chlorobenzyl)-1,6-dihydro-6-oxopyridin-3-yl)phenyl)propanoic acid
Methyl 3-(3-(1-(4-chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)propanoate
1-(4-Chlorobenzyl)-5-(4-(ethylthio)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(3-ethoxyphenyl)pyridin-2(*1H*)-one
N-(3-(1-(4-Chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)methanesulfonamide
1-(4-Chlorobenzyl)-5-(6-methoxypyridin-3-yl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-(methoxymethyl)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-((3-methoxymethyl)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(furan-3-yl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(1-benzyl-*1H*-pyrazol-4-yl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-(methylthio)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(1-methyl-*1H*-indol-5-yl)pyridin-2(*1H*)-one
tert-Butyl 2-(1-(4-chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)-*1H*-pyrrole-1-carboxylate
1-(3-Fluorobenzyl)-5-p-tolylpyridin-2(*1H*)-one
5-(4-((2H-Tetrazol-5-yl)methyl)phenyl)-1-(4-chlorobenzyl)pyridin-2(*1H*)-one
1-(3-Fluorobenzyl)-5-(2-(3-methoxyphenyl)ethynyl)pyridine-2(*1H*)-one
1-(3-Fluorobenzyl)-5-(2-(pyridin-3-yl)ethynyl)pyridin-2(*1H*)-one hydrochloride
1-(4-Chlorobenzyl)-5-(4-(methylsulfonyl)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(*1H*-indol-5-yl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-methoxyphenyl)-6-methylpyridin-2(*1H*)-one
1-(3-Fluorobenzyl)-4-phenylpyridin-2(*1H*)-one
1-(3-Fluorobenzyl)-4-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-((6-Chloropyridin-3-yl)methyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chloro-3-fluorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(3,4-Difluorobenzyl)-5-(4-(methoxymethyl)phenyl)pyridin-2(*1H*)-one
1-(3,4-Difluorobenzyl)-5-(4-acetylphenyl)pyridin-2(*1H*)-one
1-(3,4-Difluorobenzyl)-5-(2,3-dihydrobenzofuran-5-yl)pyridin-2(*1H*)-one
1-(4-Methyl-benzyl)-2-oxo-4-thiophen-2-yl-1,2-dihydro-pyridine-3-carbonitrile
1-(3,4-Difluorobenzyl)-5-(3-methoxyphenyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-(3-phenylpropyl)pyridin-2(*1H*)-one

1-(4-Fluorophenethyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-(4-phenylbutyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-hydroxyphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-((methyl(phenyl)amino)methyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-((benzyl(methyl)amino)methyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-((phenylamino)methyl)pyridin-2(*1H*)-one
(Z)-5-(3-Methoxystyryl)-1-(4-chlorobenzyl)pyridin-2(*1H*)-one
(E)-5-(3-Methoxystyryl)-1-(4-chlorobenzyl)pyridin-2(*1H*)-one
1-(3-Fluorobenzyl)-4-phenethoxypyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-isopropoxyphenyl)pyridin-2(*1H*)-one
Ethyl 2-(4-(1-(4-chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenoxy)acetate
1-(4-Chlorobenzyl)-5-((4-fluorophenyl)(hydroxy)methyl)pyridine-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-fluorobenzyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(hydroxy(3-methoxyphenyl)methyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-(2-oxo-2-phenylethyl)-*1H*-pyridin-2-one
1-((4-Chlorophenoxy)methyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-(2-phenoxyethyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-sec-butoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(3-methoxybenzoyl)pyridin-2(*1H*)-one
5-(3-Methoxyphenethyl)-1-(4-chloro-3-fluorobenzyl)pyridin-2(*1H*)-one
1-(3,4-Difluorobenzyl)-5-(3-methoxyphenethyl)pyridine-2(*1H*)-one
5-(3-Methoxybenzyl)-1-(4-chlorobenzyl)pyridin-2(*1H*)-one
1-(4-Chloro-3-fluorobenzyl)-5-(4-methoxyphenethyl)pyridine-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-methoxyphenyl)-4-methylpyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-4-methyl-5-phenylpyridin-2(*1H*)-one
1-(4-Chloro-3-fluorobenzyl)-5-(benzo[d]thiazol-2-yl)pyridin-2(*1H*)-one
1-(3,4-Difluorobenzyl)-5-(phenoxymethyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-((4-methoxyphenoxy)methyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-((4-fluorophenyl)(methyl)amino)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(phenoxymethyl)pyridin-2(*1H*)-one
1-(3,4-Difluorobenzyl)-5-(thiophen-2-yl)pyridin-2(*1H*)-one
4-(1-(3,4-Difluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)benzonitrile
N-(4-(1-(3,4-Difluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)methanesulfonamide
N-(3-Chlorobenzyl)-2-(5-(4-methoxyphenyl)-2-oxopyridin-1(2H)-yl)-N-methylacetamide
N-Benzyl-2-(5-(4-methoxyphenyl)-2-oxopyridin-1(2H)-yl)-N-methylacetamide
N-(3-Methoxybenzyl)-2-(5-(4-methoxyphenyl)-2-oxopyridin-1(2H)-yl)-N-methylacetamide
1-(3,4-Difluorobenzyl)-5-(6-methoxypyridin-3-yl)pyridine-2(*1H*)-one

1-(3,4-Difluorobenzyl)-5-(benzo[d][1,3]dioxol-5-yl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-(trifluoromethyl)phenyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(3-fluoro-4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-(Trifluoromethoxy)benzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(2,4-Difluorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(2-Methylphenylmethyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(2,3-Difluorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-4-methylquinolin-2(*1H*)-one
N-(4-Nitrobenzyl)-2-(5-(4-methoxyphenyl)-2-oxopyridin-1(2H)-yl)-N-methylacetamide
N-(4-Methylbenzyl)-2-(5-(4-methoxyphenyl)-2-oxopyridin-1(2H)-yl)-N-methylacetamide
N-(4-(Trifluoromethyl)benzyl)-2-(5-(4-methoxyphenyl)-2-oxopyridin-1(2H)-yl)-N-methylacetamide
1-(4-Chlorobenzyl)-5-phenylpyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(benzo[b]thiophen-5-yl)pyridin-2(*1H*)-one
1-(2,4,6-Trifluorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(2-Chlorobenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)pyridin-2(*1H*)-one hydrochloride
4-(1-(4-Methoxybenzyl)-6-oxo-1,6-dihydropyridin-3-yl)benzonitrile
1-(4-Methoxybenzyl)-5-(4-acetylphenyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-((6-methoxypyridin-3-yl)methyl)pyridin-2(*1H*)-one hydrochloride
1-(4-Chloro-2-fluorobenzyl)-5-(3,4-dimethoxyphenyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-((5-phenyl-1,2,4-oxadiazol-3-yl)methyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-hydroxyphenyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-(pyrrolidin-1-ylsulfonyl)phenyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-(morpholinosulfonyl)phenyl)pyridin-2(*1H*)-one
1-((4-Fluorobenzo[d]thiazol-2-yl)methyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-(2-methoxyethoxy)phenyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-bromopyridin-2(*1H*)-one
Methyl 1-(4-chlorobenzyl)-2-oxo-5-phenyl-1,2-dihydropyridine-3-carboxylate
1-(4-Chlorobenzyl)-3-(hydroxymethyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-(2-morpholinoethoxy)phenyl)pyridin-2(*1H*)-one
1-(Benzo[d]thiazol-2-ylmethyl)-5-phenylpyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-(2-(dimethylamino)ethoxy)phenyl)pyridin-2(*1H*)-one
2-(4-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenoxy)acetonitrile
5-(4-((2H-Tetrazol-5-yl)methoxy)phenyl)-1-(4-chloro-2-fluorobenzyl)pyridin-2(*1H*)-one
1-Butyl-5-(4-methoxyphenyl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(4-(3-morpholinopropoxy)phenyl)pyridin-2(*1H*)-one hydrochloride

1-(4-Chloro-2-fluorobenzyl)-5-(4-(3-(dimethylamino)propoxy)phenyl)pyridin-2(*1H*)-one

4-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl methyl carbonate

1-(4-Chloro-2-fluorobenzyl)-5-(4-(2-oxopropoxy)phenyl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(4-isobutoxyphenyl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(4-methoxy-3-methylphenyl)pyridin-2(*1H*)-one

Methyl 2-(4-(1-(4-chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenoxy)acetate

5-(4-(*1H*-Tetrazol-5-yl)phenyl)-1-(4-chloro-2-fluorobenzyl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(4-aminophenyl)pyridin-2(*1H*)-one hydrochloride

1-(4-Chloro-2-fluorobenzyl)-5-(3-aminophenyl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(4-(hydroxymethyl)phenyl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-3-fluoro-5-(4-methoxyphenyl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(4-methoxy-3,5-dimethylphenyl)pyridin-2(*1H*)-one

1-Isobutyl-5-(4-methoxyphenyl)pyridin-2(*1H*)-one

1-Isopentyl-5-(4-methoxyphenyl)pyridin-2(*1H*)-one

5-(4-Methoxyphenyl)-1-(pent-4-ynyl)pyridin-2(*1H*)-one

1-(Cyclohexylmethyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one

N-(4-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)acetamide

1-(4-Chloro-2-fluorobenzyl)-5-(4-((2-methylthiazol-4-yl)methoxy)phenyl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(4-((1-methyl-*1H*-imidazol-2-yl)methoxy)phenyl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(3,4-dihydro-2H-benzo[b][1,4]dioxepin-7-yl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(4-(2-aminoethoxy)phenyl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(4-((5-methylisoxazol-3-yl)methoxy)phenyl)pyridin-2(*1H*)-one

tert-Butyl 4-(1-(4-chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)benzylcarbamate

1-(4-Chloro-2-fluorobenzyl)-5-(4-propoxyphenyl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-4-methoxy-5-(4-methoxyphenyl)pyridin-2(*1H*)-one

N-(3-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)acetamide

1-(4-Chloro-2-fluorobenzyl)-5-(4-(aminomethyl)phenyl)pyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(3-hydroxyphenyl)pyridin-2(*1H*)-one

N-(4-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)benzyl)acetamide

N-(4-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)benzyl)methanesulfonamide

N-(3-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)benzyl)acetamide

N-(3-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)benzyl)methanesulfonamide

1-(4-Chloro-3-fluorobenzyl)-5-bromo-4-methylpyridin-2(*1H*)-one

5-(4-Methoxyphenyl)-1-((5-(trifluoromethyl)furan-2-yl)methyl)pyridin-2(*1H*)-one

1-(4-(Methoxymethyl)benzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one

1-(4-Chloro-3-fluorobenzyl)-5-bromo-4-methylpyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(4-(2-(2-oxopyrrolidin-1-yl)ethoxy)phenyl)pyridin-2(*1H*)-one

2-(4-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenoxy)-N-methylacetamide

1-(4-Chloro-2-fluorobenzyl)-5-(4-(3-aminopropoxy)phenyl)pyridin-2(*1H*)-one

1-(4-(Ethoxymethyl)benzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one

1-(4-chlorobenzyl)-5-(4-(ethoxymethyl)phenyl)pyridin-2(*1H*)-one

N-(2-(4-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenoxy)ethyl)acetamide

N-Acetyl-N-(2-(4-[1-(4-chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl]phenoxy)ethyl)acetamide

N-(2-(4-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenoxy)ethyl)methanesulfonamide

N-(3-(4-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenoxy)propyl)methanesulfonamide

N-Acetyl-N-(3-(4-(1-(4-chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenoxy)propyl)acetamide

N-(3-(4-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenoxy)propyl)acetamide

1-(4-Chloro-2-fluorobenzyl)-5-isopropylpyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(6-(dimethylamino)pyridin-3-yl)pyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(3-amino-4-methoxyphenyl)pyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(4-morpholinophenyl)pyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(5-methylthiophen-2-yl)pyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(6-morpholinopyridin-3-yl)pyridin-2(*1H*)-one

1-(4-Chloro-2-fluorobenzyl)-5-(6-methoxypyridin-3-yl)pyridin-2(*1H*)-one

5-(6-Methoxypyridin-3-yl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)pyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(4-(ethoxymethyl)phenyl)pyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(4-(benzyloxymethyl)phenyl)pyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(4-(hydroxymethyl)phenyl)pyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(4-(dimethylamino)phenyl)pyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(quinoxalin-6-yl)pyridin-2(*1H*)-one

Methyl 4-(1-(4-chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)benzoate

1-(4-Chlorobenzyl)-5-(4-(3-hydroxypropyl)phenyl)pyridin-2(*1H*)-one

4-(1-Isopentyl-6-oxo-1,6-dihydropyridin-3-yl)benzonitrile

N-(3-(1-Isopentyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl)methanesulfonamide

3-(1-(4-Chloro-2-fluorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)benzonitrile
1-(4-Chlorobenzyl)-5-(4-methoxyphenyl)pyrazin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(6-chloropyridin-3-yl)pyridin-2(*1H*)-one
N-(5-(1-(4-Chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)-2-methoxyphenyl)methanesulfonamide
5-(4-Methoxyphenyl)-1-pentylpyridin-2(*1H*)-one
1-(Cyclopropylmethyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-(4,4,4-trifluorobutyl)pyridin-2(*1H*)-one
1-(Cyclopentylmethyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
Methyl 2-(4-(1-(4-chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)acetate
1-(4-Chlorobenzyl)-5-cyclohexylpyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(quinolin-7-yl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-(furan-2-ylmethoxy)phenyl)pyridin-2(*1H*)-one
5-(3-(2H-Tetrazol-5-yl)phenyl)-1-(4-chloro-2-fluorobenzyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-(2-hydroxypropan-2-yl)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-(isobutoxymethyl)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-phenylpyrazin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-((2-(dimethylamino)ethoxy)methyl)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-((2-morpholinoethoxy)methyl)phenyl)pyridin-2(*1H*)-one
2-(4-(1-(4-Chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)acetic acid
4-(1-(4-Chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)-N,N-dimethylbenzamide
2-(4-(1-(4-Chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)-N,N-dimethylacetamide
N-(2-(4-(1-(4-chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)benzyloxy)ethyl)acetamide
1-(4-Chlorobenzyl)-5-(4-((2-methoxyethoxy)methyl)phenyl)pyridin-2(*1H*)-one
1-(4-Fluorobenzyl)-4-(furan-2-yl)-2-oxo-1,2-dihydropyridine-3-carbonitrile
2-(4-(1-(4-Chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)-N-methylacetamide
3-(4-(1-(4-Chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)-N-methylpropanamide
3-(4-(1-(4-Chlorobenzyl)-6-oxo-1,6-dihydropyridin-3-yl)phenyl)-N,N-dimethylpropanamide
1-(4-Chloro-2-fluorobenzyl)-5-(4-(2-hydroxypropoxy)phenyl)pyridin-2(*1H*)-one
1-Isopentyl-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridine-3-carbonitrile
2-Oxo-1-(3-phenylpropyl)-4-(thiophen-2-yl)-1,2-dihydropyridine-3-carbonitrile
4-(Furan-2-yl)-1-isopentyl-2-oxo-1,2-dihydropyridine-3-carbonitrile
4-(Furan-2-yl)-2-oxo-1-(3-phenylpropyl)-1,2-dihydropyridine-3-carbonitrile
1-(4-Methylphenylmethyl)-4-(furan-2-yl)-2-oxo-1,2-dihydropyridine-3-carbonitrile
1-(4-Chloro-2-fluorobenzyl)-5-(3-phenylpropyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-(3-methoxyphenyl)butyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-phenylbutyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-butylpyridin-2(*1H*)-one

1-(4-Chlorobenzyl)-5-(4-methoxyphenyl)pyrimidin-2(*1H*)-one
1-Benzyl-5-(4-methoxyphenyl)pyrimidin-2(*1H*)-one
1-Isopentyl-5-(4-methoxyphenyl)pyrazin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-(2-(dimethylamino)ethylamino)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-(2-methoxyethylamino)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-(propylamino)phenyl)pyridin-2(*1H*)-one
1-(3,3-Dimethylbutyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-(pyridin-3-ylmethoxy)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-4-(2-hydroxyethyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-(4-methoxyphenyl)butyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-methoxybenzyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(3-phenoxypropyl)pyridin-2(*1H*)-one
1-Isopentyl-4-methylquinolin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-methoxyphenoxy)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-propoxypyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(cyclohexylmethoxy)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-fluorobenzyloxy)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-methoxybenzyloxy)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-phenethoxypyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(4-fluorophenoxy)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(2-methoxyethoxy)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(5-methylpyridin-2-yl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-(4-(pyridin-2-ylmethoxy)phenyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-4-(methoxymethyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-4-(2-methoxyethyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-3-chloro-5-phenylpyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-3-methoxy-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
5-(2-Methoxybenzyl)-1-(4-chloro-2-fluorobenzyl)pyridin-2(*1H*)-one
N-(3-(1-(4-Chlorobenzyl)-5-chloro-6-oxo-1,6-dihydropyridin-3-yl)phenyl)acetamide
5-(4-Methoxyphenethylamino)-2-propylisoquinolin-1(2H)-one
5-(4-Hydroxyphenethylamino)-2-propylisoquinolin-1(2H)-one
1-(4-Chlorobenzyl)-6-methoxy-4-methylquinolin-2(*1H*)-one
1-Isobutyl-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridine-3-carbonitrile
1-(Cyclohexylmethyl)-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridine-3-carbonitrile
2-Oxo-4-(thiophen-2-yl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)-1,2-dihydropyridine-3-carbonitrile
5-(4-Methoxyphenyl)-1-((6-(4-methoxyphenyl)pyridin-3-yl)methyl)pyridin-2(*1H*)-one
1-((6-Ethynylpyridin-3-yl)methyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-((6-Ethylpyridin-3-yl)methyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one

2-Oxo-1-(pentan-2-yl)-4-(thiophen-2-yl)-1,2-dihydropyridine-3-carbonitrile
5-(4-Methoxyphenyl)-1-((2-methylthiazol-5-yl)methyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-((5-methylpyrazin-2-yl)methyl)pyridin-2(*1H*)-one
5-(Phenoxymethyl)-1-((6-(trifluoromethyl)pyridin-3-yl)methyl)pyridin-2(*1H*)-one
mixture of isomers of 1-(4-chloro-2-fluorobenzyl)-5-(4-((2-methyl-2H-tetrazol-5-yl)methoxy)phenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-3-chloro-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
N-(3-(5-Chloro-1-isopentyl-6-oxo-1,6-dihydropyridin-3-yl)phenyl)methanesulfonamide
1-(4-Chlorobenzyl)-5-(4-fluorophenyl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-(pentan-2-yl)pyridin-2(*1H*)-one
5-(4-Methoxyphenyl)-1-((4-methylcyclohexyl)methyl)pyridin-2(*1H*)-one
1-Isopentyl-2-oxo-4-phenyl-1,2-dihydropyridine-3-carbonitrile
4-(Benzo[d][1,3]dioxol-5-yl)-1-isopentyl-2-oxo-1,2-dihydropyridine-3-carbonitrile
1-(4-Ethoxybenzyl)-5-(4-methoxyphenyl)pyridin-2(*1H*)-one
1-Isopentyl-5-(4-methoxyphenyl)pyrimidin-2(*1H*)-one
1-Isopentyl-5-((4-methoxyphenoxy)methyl)pyridin-2(*1H*)-one
1-(4-Chloro-2-fluorobenzyl)-5-((3-methoxyphenoxy)methyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(2-fluoro-4-methoxyphenyl)pyridin-2(*1H*)-one
1-(4-Chlorobenzyl)-5-(2-methoxypyrimidin-5-yl)pyridin-2(*1H*)-one
2-Oxo-1-propyl-4-(thiophen-2-yl)-1,2-dihydropyridine-3-carbonitrile
1-Butyl-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridine-3-carbonitrile
1-(2-Methylbutyl)-2-oxo-4-phenyl-1,2-dihydropyridine-3-carbonitrile
1-(4-Chlorobenzyl)-2-oxo-4-(thiophen-2-yl)-1,2-dihydropyridine-3-carbonitrile
6-Chloro-1-isopentylquinolin-2(*1H*)-one
4-(4-Methoxyphenethyl)-2-propylisoquinolin-1(2H)-one
5-(4-Methoxyphenethoxy)-2-propylisoquinolin-1(2H)-one.

DEFINITION OF TERMS

Listed below are definitions of various terms used in the specification and claims to describe the present invention.

For the avoidance of doubt it is to be understood that in this specification "(C_1-C_6)" means a carbon radical having 1, 2, 3, 4, 5 or 6 carbon atoms. "(C_0-C_6)" means a carbon radical having 0, 1, 2, 3, 4, 5 or 6 carbon atoms. In this specification "C" means a carbon atom, "N" means a nitrogen atom and "S" means a sulphur atom.

In the case where a subscript is the integer 0 (zero) the radical to which the subscript

refers, indicates that the radical is absent, i.e. there is a direct bond between the radicals.

When two or more bonds are adjacent to one another, they are assumed to be equal to one bond. For example, a radical -A-B-, wherein both A and B may be a bond, the radical is depicting a single bond.

In this specification, unless stated otherwise, the term "bond" refers to a saturated covalent bond.

In this specification, unless stated otherwise, the term "alkyl" includes both straight and branched chain alkyl radicals and may be methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, i-pentyl, t-pentyl, neo-pentyl, n-hexyl or i-hexyl, t-hexyl. The term "(C_0-C_3)alkyl" refers to an alkyl radical having 0, 1, 2 or 3 carbon atoms, and may be methyl, ethyl, n-propyl and i-propyl.

In this specification, unless stated otherwise, the term "cycloalkyl" refers to an optionally substituted carbocycle containing no heteroatoms, including mono-, bi-, and tricyclic saturated carbocycles, as well as fused ring systems. Such fused ring systems can include one ring that is partially or fully unsaturated such as a benzene ring to form fused ring systems such as benzo- fused carbocycles. Cycloalkyl includes such fused ring systems as spirofused ring systems. Examples of cycloalkyl include cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, decahydronaphthalene, adamantane, indanyl, fluorenyl, 1,2,3,4-tetrahydronaphthalene and the like. The term "(C_3-C_7)cycloalkyl" may be cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and the like.

In this specification, unless stated otherwise, the term "alkenyl" includes both straight and branched chain alkenyl radicals. The term "(C_2-C_6)alkenyl" refers to an alkenyl radical having 2 to 6 carbon atoms and one or two double bonds, and may be, but is not limited to vinyl, allyl, propenyl, i-propenyl, butenyl, i-butenyl, crotyl, pentenyl, i-pentenyl and hexenyl.

In this specification, unless stated otherwise, the term "alkynyl" includes both straight and branched chain alkynyl radicals. The term (C_2-C_6)alkynyl having 2 to 6 carbon atoms and one or two triple bonds, and may be, but is not limited to ethynyl, propargyl, butynyl, ibutynyl, pentynyl, i-pentynyl and hexynyl.

The term "aryl" refers to an optionally substituted monocyclic or bicyclic hydrocarbon ring system containing at least one unsaturated aromatic ring. Examples and suitable values of the term "aryl" are phenyl, naphtyl, 1,2,3,4-tetrahydronaphthyl, indyl , indenyl and the like.

In this specification, unless stated otherwise, the term "heteroaryl" refers to an optionally substituted monocyclic or bicyclic unsaturated, aromatic ring system containing at least one heteroatom selected independently from N, O or S. Examples of "heteroaryl" may be, but are not limited to thiophene, thienyl, pyridyl, thiazolyl, isothiazolyl, furyl, pyrrolyl, triazolyl, imidazolyl, oxadiazolyl, oxazolyl, isoxazolyl, pyrazolyl, imidazolonyl, oxazolonyl, thiazolonyl, tetrazolyl and thiadiazolyl, benzoimidazolyl, benzooxazolyl, benzothiazolyl, tetrahydrotriazolopyridyl, tetrahydrotriazolopyrimidinyl, benzofuryl, thionaphtyl, indolyl, isoindolyl, pyridonyl, pyridazinyl, pyrazinyl, pyrimidinyl, quinolyl, , phtalazinyl, naphthyridinyl, quinoxalinyl, quinazolyl, imidazopyridyl, oxazolopyridyl, thiazolopyridyl, pyridyl, imidazopyridazinyl, oxazolopyridazinyl, thiazolopyridazinyl, cynnolyl, pteridinyl, furazanyl, benzotriazolyl, pyrazolopyridinyl, purinyl and the like.

In this specification, unless stated otherwise, the term "alkylaryl", "alkylheteroaryl" and "alkylcycloalkyl" refers respectively to a substituent that is attached via the alkyl radical to an aryl, heteroaryl or cycloalkyl radical, respectively. The term "(C_1-C_6)alkylaryl" includes aryl-C_1-C_6-alkyl radicals such as benzyl, 1-phenylethyl, 2-phenylethyl, 1-phenylpropyl, 2-phenylpropyl, 3-phenylpropyl, 1-naphtylmethy, 2-naphtylmethyl, or the like. The term "(C_1-C_6)alkyheteroaryl" includes heteroaryl-C_1-C_3-alkyl radicals, wherein examples of heteroaryl are the same as those illustrated in the above definition, such as 2-furylmethyl, 3-furylmethyl, 2-thienylmethyl, 3-thienylmethyl, 1-imidazolylmethyl, 2-imidazolylmethyl, 2-thiazolylmethyl, 2-pyridylmethyl, 3-pyridylmethyl, 1-quinolylmethyl, or the like.

In this specification, unless stated otherwise, the term "heterocycle" refers to an optionally substituted, monocyclic or bicyclic saturated, partially saturated or unsaturated ring system containing at least one heteroatom selected independently from N, O and S.

In this specification, unless stated otherwise, a 5- or 6-membered ring containing one or

more atoms independently selected from C, N, O and S, includes aromatic and heteroaromatic rings as well as carbocyclic and heterocyclic rings which may be saturated or unsaturated. Examples of such rings may be, but are not limited to, furyl, isoxazolyl, isothiazolyl, oxazolyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, thiazolyl, thienyl, imidazolyl, imidazolidinyl, imidazolinyl, triazolyl, morpholinyl, piperazinyl, piperidyl, piperidonyl, pyrazolidinyl, pyrazolinyl, pyrrolidinyl, pyrrolinyl, tetrahydropyranyl, thiomorpholinyl, phenyl, cyclohexyl, cyclopentyl, cyclohexenyl, and the like.

In this specification, unless stated otherwise, a 3- to 10-membered ring containing one or more atoms independently selected from C, N, O and S, includes aromatic and heteroaromatic rings as well as carbocyclic and heterocyclic rings which may be saturated or unsaturated. Examples of such rings may be, but are not limited to imidazolidinyl, imidazolinyl, morpholinyl, piperazinyl, piperidyl, piperidonyl, pyrazolidinyl, pyrazolinyl, pyrrolidinyl, pyrrolinyl, tetrahydropyranyl, thiomorpholinyl, tetrahydrothiopyranyl, furyl, pyrrolyl, isoxazolyl, isothiazolyl, oxazolyl, oxazolidinonyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, thiazolyl, thienyl, imidazolyl, triazolyl, phenyl, cyclopropyl, aziridinyl, cyclobutyl, azetidinyl, cyclopentyl, cyclopentenyl, cyclohexyl, cyclohexenyl, cycloheptyl, cycloheptenyl, cyclooctyl , cyclooctenyl, and the like.

In this specification, unless stated otherwise, the term "halo" may be fluoro, chloro, bromo or iodo.

In this specification, unless stated otherwise, the term "alkylhalo" means an alkyl radical as defined above, substituted with one or more halo radicals. The term "(C_1-C_6)alkylhalo" may include, but is not limited to, fluoromethyl, difluoromethyl, trifluoromethyl, fluoroethyl and difluoroethyl. The term "O-C_1-C_6-alkylhalo" may include, but is not limited to, fluoromethoxy, difluoromethoxy, trifluoromethoxy and fluoroethoxy.

In this specification, unless stated otherwise, the term "alkylcyano" means an alkyl radical as defined above, substituted with one or more cyano.

(This paragraph will be cleaned up tomorrow)

In this specification, unless stated otherwise, the term "optionally substituted" refers to radicals further bearing one or more substituents which are preferably selected from the group of (C_1-C_6)alkyl; (C_1-C_6)alkyloxy; hydroxy(C_1-C_6)alkyloxy; (C_1-C_6)alkyloxy(C_1-C_6)alkyl; (C_1-C_6)alkyloxy(C_1-C_6)alkyloxy; (C_1-C_6)alkyloxycarbonyl; (C_1-C_6)alkyloxycarbonyl(C_1-C_6)alkyl; (C_1-C_6)alkyloxycarbonyloxy; (C_1-C_6)alkyloxycarbonyl(C_1-C_6)alkyloxy; (C_1-C_6)alkylcarbonyl; (C_1-C_6)alkylcarbonyl(C_1-C_6)alkyloxy; (C_1-C_6)alkylcarbonyloxy; (C_1-C_6)alkylthieno; (C_1-C_6)alkylsulfonyl; heterocyclic-sulfonyl, preferably morpholinylsulfonyl and pyrrolidinylsulfonyl; (C_1-C_6)alkylsulfonylamino; (C_1-C_6)alkenyl; aryl, preferably phenyl; carboxyl(C_1-C_6)alkyl; carbonyl(C_1-C_6)alkyloxy; halo, preferably fluoro and chloro; hydroxy; hydroxy(C_1-C_6)alkyl; phenyl(C_1-C_6)alkyloxy; cyano; cyano(C_1-C_6)alkyloxy; trifluoro(C_1-C_6)alkyl; trifluoro(C_1-C_6)alkyloxy; amino; amino(C_1-C_6)alkyloxy; mono- and di((C_1-C_6)alkyl)amino; mono- and di((C_1-C_6)alkylcarbonyl)amino; mono- and di((C_1-C_6)alkyloxycarbonyl)amino; mono- and di((C_1-C_6)alkylcarbonyl)amino(C_1-C_6)alkyl; mono- and di((C_1-C_6)alkylsulfonyl)amino(C_1-C_6)alkyloxy; mono- and di((C_1-C_6)alkyl)amino(C_1-C_6)alkyloxy; mono- and di((C_1-C_6)alkylcarbonyl)amino(C_1-C_6)alkyloxy; mono- and di((C_1-C_6)alkyl)aminocarbonyl; mono- and di((C_1-C_6)alkyl)aminocarbonyl(C_1-C_6)alkyl; mono- and di((C_1-C_6)alkyl)aminocarbonyl(C_1-C_6)alkyloxo; mono- and di((C_1-C_6)alkyl)amino(C_1-C_6)alkylamino; nitro; tri(C_1-C_6)alkylsilyl; heterocyclic, preferably morpholinyl; heterocyclic-(C_1-C_6)alkyl, preferably (C_1-C_6)alkyltetrazolyl; and heterocyclic-(C_1-C_6)alkyloxy, the heterocyclic preferably being pyridinyl, morpholinyl, pyrrolidinyl, optionally substituted with oxo, isoxazolyl, imidazolyl, tetrazolyl or thiazolyl.

In this specification, the term "solvate" refers to a complex of variable stoichiometry formed by a solute (e.g. a compound of Formula (I)) and a solvent. The solvent is a pharmaceutically acceptable solvent as preferably water ; such solvent may not interfere with the biological activity of the solute.

In this specification, unless stated otherwise, the term "positive allosteric modulator of mGluR2" or "allosteric modulator of mGluR2" refers also to a pharmaceutically acceptable acid or base addition salt thereof, a stereochemically isomeric form thereof and an *N*-oxide form thereof.

PHARMACEUTICAL COMPOSITIONS

Positive allosteric modulators of mGluR2 described herein, and the pharmaceutically acceptable salts, solvates and hydrates thereof can be used in pharmaceutical preparations in combination with a pharmaceutically acceptable carrier or diluent. Suitable pharmaceutically acceptable carriers include inert solid fillers or diluents and sterile aqueous or organic solutions. The positive allosteric modulators of mGluR2 will be present in such pharmaceutical compositions in amounts sufficient to provide the desired dosage amount in the range described herein. Techniques for Formulation and administration of the compounds of the instant invention can be found in *Remington: the Science and Practice of Pharmacy*, 19th edition, Mack Publishing Co., Easton, PA (1995).

The amount of positive allosteric modulators of mGluR2, administered to the subject will depend on the type and severity of the disease or condition and on the characteristics of the subject, such as general health, age, sex, body weight and tolerance to drugs. The skilled artisan will be able to determine appropriate dosages depending on these and other factors. Effective dosages for commonly used CNS drugs are well known to the skilled person. The total daily dose usually ranges from about 0.05 – 2000 mg.

The present invention relates to pharmaceutical compositions which provide from about 0.01 to 1000 mg of the active ingredient per unit dose. The compositions may be administered by any suitable route. For example orally in the form of capsules, etc..., parenterally in the form of solutions for injection, topically in the form of onguents or lotions, ocularly in the form of eye-drops, rectally in the form of suppositories, intranasally or transcutaneously in the form of delivery system like patches.

For oral administration, the positive allosteric modulators of mGluR2 thereof can be combined with a suitable solid or liquid carrier or diluent to form capsules, tablets, pills, powders, syrups, solutions, suspensions and the like.

The tablets, pills, capsules, and the like contain from about 0.01 to about 99 weight percent of the active ingredient and a binder such as gum tragacanth, acacias, corn starch or gelatin; excipients such as dicalcium phosphate; a disintegrating agent such as